University of Alberta

ANALYSIS OF HEALTH RISK EVIDENCE AND INFERENCE IN CANADA

by

Simon Philip Thomas

A thesis submitted to the Faculty of Graduate Studies and Research in partial fulfillment of the requirements for the degree of Master of Science

in

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ABSTRACT

Information from a diverse range of health related fields is used to communicate health risks to professionals and the public. The purpose of this thesis is to provide a summary of currently accessible health risk evidence information to aid in communicating health risks. This will be accomplished by providing not just the information but also an explanation of the source (evidentiary and inferential basis) and the certainty of the information. Health risk information has been separated into three categories: direct, indirect and predictive. Direct evidence is taken from death certificates which include the age, gender and cause of death. Indirect evidence and inference is based on epidemiological studies which are used to estimate risk factors. Predictive inference is based on toxicological risk assessment and uses extrapolation of experimentally determined dose-response relationships in laboratory animals to estimate human health risk.

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1. INTRODUCTION

1.1 Purpose

The basis of this thesis is a perceived lack of accessibility to and general understanding of relevant health risk information in society. The purpose of this thesis is to provide a summary of health risk information and more importantly an explanation of where and how this information is derived.

A difficulty with health risks is the broad range of health risks and enormous amount of available information. The following quote, though referring to Americans applies equally well in Canada:

> "As a society and as individuals, we Americans are preoccupied with risks, particularly risks to life. From AIDS to cancer to heart disease, from Alar to asbestos to benzene, from eating to drinking to smoking - we worry about all the risks of living ... We cannot banish these risks, but we can and should learn better ways to deal with them. Dealing better with risks means worrying less and thinking more so that we make better-informed decisions about them." (Keeney, 1994, pg. 193)

This quote highlights the broad range of health risks including major causes of death, lifestyle factors and chemicals in the environment. It also suggests that these risks can be dealt with better to make more informed decisions. To help individuals make more informed decisions, information which is relevant to individuals is required.

Relevant information on health risks involves more than just presenting a probability estimate of the risk, it also requires an explanation of the evidence and inferential basis used to develop the information, the certainty of the information and the confidence individuals may place in it. Therefore to accomplish the purpose of this thesis, two goals must be achieved:

1. to provide a summary of accessible health risk information, and
2. to provide an explanation of the source (evidence and inferential basis) and certainty of this information.

A difficulty with the first goal, of providing a summary of accessible health risk information, is that even a summary could easily be many volumes long. For this reason, priority was placed on limiting the total amount of information to:

- focus on human health risks not other animals or the environment (noting environmental risks to humans are included)
- focus on mortality information (discussed later in more detail, but mortality information provides the base)
- focus on Canadian information (where possible)

The goal of providing information which allows people to inform themselves about health risks is different from telling people what to do about the them. In a book called "Living with Risk" the British Medical Association, in addition to highlighting the need for information, makes an important statement on the impartiality of the information:

> "In order to make sensible decisions about the risks we run in our present way of life, we need information. To provide it is the purpose of this book. To the extent that available data permit, it represents an attempt to put risk in perspective, and to put numbers on a selection of risks as far as is possible. It is not its purpose to make choices for people, but only to present some of the facts on which those choices may be based." (British Medical Association, 1987, pg. x)

No data summary, including this thesis, can claim to present only impartial information which is totally free from bias. However, no conscious attempts were made to select information which would support any particular actions or behaviours. To the greatest extent possible, this thesis attempts to provide data to inform the reader with a range of perspectives so that whatever conclusions a reader might reach will be based on an accurate understanding of the available evidence.

The second goal of this thesis is to provide an explanation of the source and the certainty of the information presented. The two ideas of source of evidence and uncertainty in knowledge are closely linked. Currently, most published health risk information does not include an estimate or explanation of the uncertainty inherent in numerical estimates or causal inferences. Because quantitative estimates of uncertainty are not readily available, a different, more general approach was used to estimate the uncertainty.

Uncertainty comes from how the information is measured and how it is interpreted. If basic information can be measured accurately, is comprehensive in its coverage (e.g. death registration in Canada) and does not require substantial inference to link measurement with interpretation then it will have a low uncertainty and vice versa. Based on this premise, the main source of the information was used as a basis for explaining the uncertainty. By focusing on the source, a more detailed analysis of how the information is measured can be made. With this approach, the range of the uncertainty can be estimated even if the information from a given source is presented without mention of uncertainty.

The rest of this introduction is separated into four sections. The first describes in more detail the three categories of information that have been developed based on the source of the information. These categories, direct, indirect and predictive are the titles of the second, third and fourth sections of this thesis. The second section in this introduction is an evaluation of the components of health risk information. These include definitions of health and risk as well as a review of risk perception. The third section in this introduction is a review of areas of literature that were used in this thesis with mention of particularly relevant and important sources. The fourth and final section in this introduction discusses several topics relating to interpreting numbers.

1.2 Categories of Health Risk Information

Three categories are being used to divide the mortality based health risk information. The categories were selected after reviewing readily available health risk information in Canada. Based on this review, direct evidence from death certificates, indirect evidence and inference from epidemiology and predictive inference from toxicological risk assessment were identified as the three categories. Each category is dealt with in a separate section. These sections will be introduced here to explain the similarities and differences between them. In the fifth section of this thesis, the discussion, a more detailed comparison of the three categories is provided.

Direct evidence is based on evidence collected and summarized from death certificates which are completed for everyone who dies in Canada. This evidence is collected from across Canada and published annually by Statistics Canada along with other reports on vital statistics. Key components of direct evidence are the age and gender of the individual and always present for death certificates, the cause of death.

Indirect evidence and inference is based on epidemiological studies designed to determine risk factors relating to health risks. Unlike direct evidence, where all the evidence is related to mortality, epidemiological studies can address non-lethal (morbidity) health conditions. For most risk factors the indirect evidence and inference was not specific to Canada because a limited number of epidemiological studies have been performed on Canadians. For these risk factors, evidence and inference from similarly developed countries can be used.

Predictive inference is based on toxicological risk assessment of specific chemicals and compounds. Estimates of health risk to humans can be generated for certain types of chemicals. The current toxicological risk assessment protocols only perform a probability estimate of risk for carcinogens. For non-carcinogens risk estimates are mainly limited to providing estimated levels below which adverse health effects are not expected. Predictive estimates of risk are usually based on the results of animal studies which then are extrapolated to humans.

Table 1.1 identifies several items that help to distinguish the three categories of health risk evidence and inference.

Table 1.1 Three Categories of Health Risk Evidence and Inference

The knowledge in the three categories is based on evidence, inference or a combination of both. Evidence is information measured for the individual. Inference is information extrapolated from what is measured, to the general population. Coverage refers to how much of the affected population is measured in the health risk information. For direct evidence, all the values that are published are based on individual measurement of each person involved and includes everyone who dies (with very small, relatively insignificant exceptions). Indirect evidence and inference is based on a selected sample of the population, consequently, how representative the sample is will determine the applicability of the findings to people outside the sample. Predictive inference is usually based on studies in animals and an estimate of exposure in humans which must also be representative of actual exposures. While animal models cannot be as representative as human population samples, laboratory experiments with animal models can be more closely controlled than observations of human populations.

There are several other sources of evidence which are similar to direct evidence but which are not based on death certificates. Some more widely distributed examples include hospital discharge records, the Canadian Cancer registry, Transport Canada tracking of all motor vehicle accidents, Workers Compensation tracking injuries and fatalities on the job. All these sources are based on a one person-one record direct approach.

There is an important and fundamental difference between both direct and indirect evidence and predictive inference. Both direct and indirect evidence begin with the existence of an effect and seek to determine the cause (e.g. what caused the death, does diet affect heart disease). Even cohort epidemiological studies which gather potential causal evidence while following a cohort for the appearance of effects are based on the knowledge that some relevant effects will arise in the cohort. However, predictive toxicology begins with a cause and seeks to determine what effect will arise.

Table 1.1 Three Categories of Health Risk Evidence and Inference

Factor	DIRECT	INDIRECT	PREDICTIVE
Source	Death certificates	Epidemiological studies	Toxicological risk assessment
Knowledge Based On	Evidence	Evidence and Inference	Inference
Coverage	Everyone	Population sample	Experimental laboratory animals
Type of Information	Age, gender and cause of death	Association between exposure and effect for exposure to a risk factor	Estimate of risk associated with specific exposure

1.3 Health Risk Evidence and Inference

1.3.1 Health

The World Health Organization established a comprehensive definition of health almost 50 year ago: "health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity." (Beaglehole et al., 1993, pg. 13)

While the focus of this thesis is on mortality, it does not mean that only the physical aspects are considered. While direct evidence, based on death certificates, is only physically expressed, risk factors associated with mortality include mental and social aspects as well.

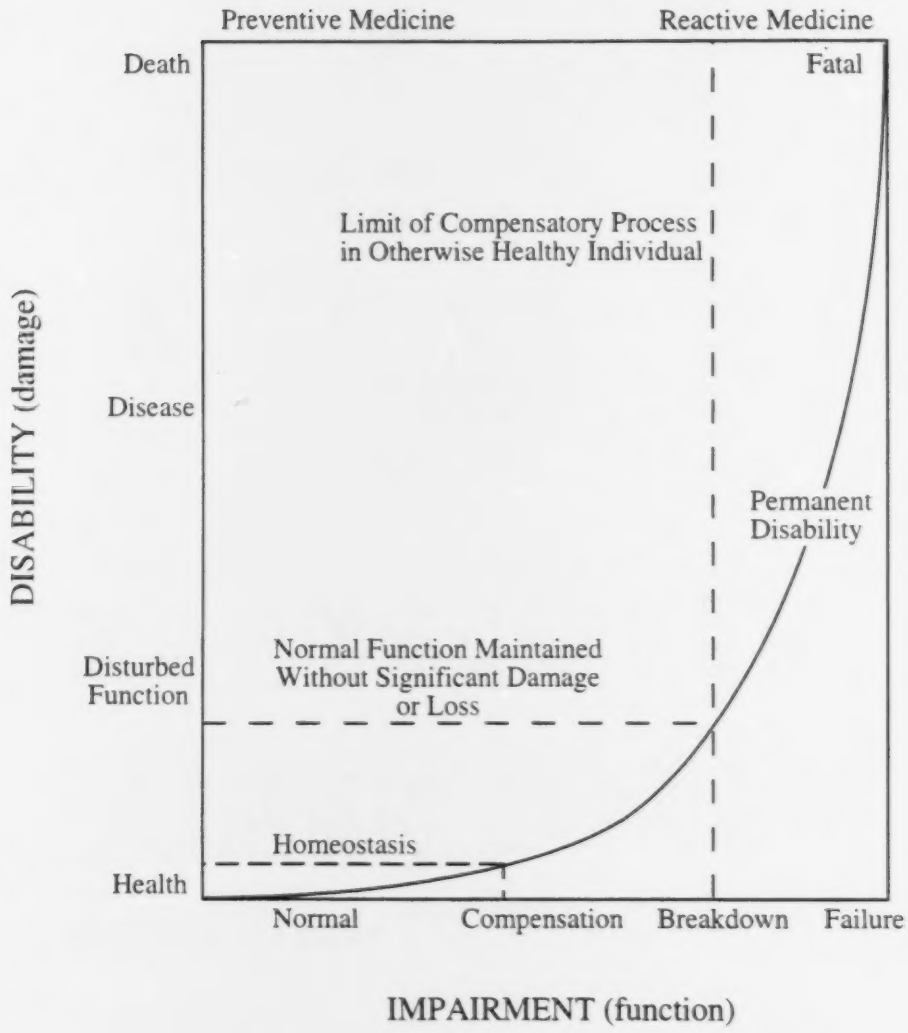
There is not a simple distinction between healthy and unhealthy. Health is a continuum from an ideal state of health to death. Figure 1.1 demonstrates this by showing health as a function of impairment and disability. The vertical, disability axis goes from health to death and the horizontal, impairment axis goes from normal to failure. The box in the lower left corner is homeostasis, where the body is in good health. Throughout life people move back and forth along this line. Depending on the cause of death, they may gradually move to the right of the line over the course of months or they may move along the line in a matter of seconds (e.g. fatal injuries).

Figure 1.1 Disability versus Impairment

Two important points about health are demonstrated in Figure 1.1. The first, which has been explained, is that health is a continuum not a dichotomy of healthy and unhealthy. The second is that health is dynamic, because an individuals health status can move back and forth along the line during a lifetime. Both of these points highlight the great difficulty in summarizing health measures for a population.

Given these complications, indicators, like those related to mortality (e.g. life expectancy, age-standardized death rates) are often used. Other indicators include hospital admission rates and national surveys of common risk factors (e.g. smoking, alcohol consumption, economic status).

Figure 1.1 Disability versus Impairment



Adapted from Hatch, 1962, Figure 2

1.3.1.1 Mortality

The base of the information presented in this thesis is mortality data. As William Rowe put it:

> "The only certainty in life is death; uncertainty lies in when and how death occurs, and whether it is final. Man strives to delay its onset and extend the quality of life in the interim. Threats to these objectives involve risks, some natural, some man-made, some beyond our control, and some controllable." (Rowe, 1977, pg. 1)

Since explaining the uncertainty associated with health risk evidence and inference is a major goal of this thesis, it is logical that it starts from the only certain piece of health risk information - death. Unfortunately most people concerned with health risks do not only want to know that they will die, as Rowe puts it, people want to know the when and how. Ultimately, most people want to know how to delay the inevitable as long as possible.

Starting from a death, a whole and complicated series of "causes" can be associated with it trying to explain how someone died. Identifying causes of death can be done in several ways. When someone states the cause of death, they have selected one of these ways. Ultimately, everyone dies of the same final cause, the heart stops beating, and oxygen is no longer supplied to the body causing death.

For this thesis, the cause of death referred to will be what was reported on the death certificate, the most 'direct' link to the actual death which is widely available. Even in this case however a selection is being made because multiple medical factors often contribute to a death. Epidemiological evidence and inference is sometimes used to estimate the cause of death from particular risk factors and toxicological risk assessment estimates the number of cancers caused from a particular exposure to a chemical. Unfortunately, these causes are often equated with those from the death certificate, which is why one of the purposes of this thesis is to explain the uncertainties based on the source of the knowledge.

While this thesis focuses mainly on mortality, this focus occurs mostly in the direct evidence section. In the direct evidence section so much health data was available that limiting consideration to mortality was required. In epidemiological studies, sometimes cancer incidence or some other measure of morbidity is used instead of mortality. For predictive inference, all the risk estimates are for cancer incidence, not mortality. Fortunately there is a fairly well established relationship between cancer incidence and mortality which is presented in the direct evidence section along with cancer mortality.

By focusing on mortality, a complete picture of health is not achieved. While mortality is a useful indicator for many of the most important health risks like cardiovascular disease, cancer, respiratory disease and fatal injuries it is less useful for several others. These involve many conditions which have a high incidence (i.e. are common) but low mortality: colds, asthma, arthritis, mental conditions, non-fatal injuries, malnutrition, dental health, etc. To highlight the enormous difference between the volume of mortality and non-mortality information note that in any given day for every person who dies, approximately 20 are admitted to hospital and 800 consult a health professional (Shah, 1994, pg. 103).

The subject of death is a very personal and often painful experience. This thesis does not attempt to personalize the facts and figures. Only recently has there been more widespread research into the social aspects of death and dying. Kubler-Ross has been an active promoter of this subject for several decades and her work has eventually lead to university courses on death and dying accompanied by comprehensive textbooks (e.g. DeSpelder et al., 1992). In a best-selling book called "How We Die" the physician Robert Nuland provides a compassionate and personal outlook of dying from an insiders point of view:

> "Every life is different from any that has gone before it, and so is every death. The uniqueness of each of us extends even to the way we die. Though most people know that various diseases carry us to our final hours by various paths, only very few comprehend the fullness of that endless multitude of ways by which the final forces of the human spirit can separate themselves from the body. Every one of death's diverse appearances is as distinctive as that singular face we each show the world during the days of life. Every man will yield up the ghost in a manner that the heavens have never know before: every woman will go her final way in her own way." (Nuland, 1993, pg. 3)

1.3.2 Risk

The concept of risk, and quantifying risk can be traced back to the seventeenth century when it was discovered that mathematics, and specifically probability theory, could be used to estimate the odds (the probability component of risk) in games of chance (gambling) (Trefil, 1984). This evolved to the point where a whole industry, insurance, is now based on their ability to predict risks.

Defining risk is a study of its own. Hrudey (1996a) has developed a notion of risk that combines and expands on previous attempts at defining risk (Kaplan et al., 1981; Renn, 1992). Hrudey defines risk as a prediction involving:

- a hazard (the source of danger)
- uncertainty of occurrence and outcomes (expressed by probability distributions)
- adverse consequences (the possible outcomes)
- a time frame for evaluation
- the perspectives of those affected

This thesis adopts but limits the focus of this definition in several ways. The hazards are the various causes of health risks. Where possible these will focus on Canadian data. The uncertainty of occurrence and outcomes is limited to point estimates of probability by the available information. The adverse consequences are focusing on, but not limited to mortality outcomes. The time frame for evaluation varies with the source of the data with annual and lifetime risk being the most commonly used. The perspectives of those affected is beyond the scope of this thesis but the issue of risk perception is touched upon lightly in Section 1.3.3.

Mortality risk is defined for this thesis as the probability of the specific outcome (death) with corresponding consideration of the cause and uncertainty in the estimated probability. The definition can be easily modified to cancer risk by using cancer instead of mortality and death.

Mortality Risk = Probability of Death (from a specific cause and/or factor within a time period) Including Uncertainty in the Probability Prediction

Probability of death has two parts that must be included in addition to the numerical estimate. First is specifying which specific cause and/or factors are involved and the second is what time frame is the being used (e.g. annual or lifetime).

The following sub-sections describe probability and uncertainty in more detail. One difficulty when dealing with probability and uncertainty is that the different categories of health risk evidence and inference use different terms to describe uncertainty. In direct evidence, terms like errors and accuracy are often used. In indirect evidence and inference,

terms like bias and confounding are used. Most of the work on defining probability and uncertainty has been generated from research on predictive inference. This makes sense because uncertainty in predictive inferences are often so large as to overwhelm the most plausible estimates.

1.3.2.1 Probability

Similar to the words health and risk, probability has different uses in different contexts. A misunderstanding of mortality risk is often associated with a misunderstanding of probability. Kleindorfer et al. (1993) described three schools of probability: classical, frequency and subjective.

The classical school defines probability as the number of favourable outcomes divided by the total number of possible outcomes a definition which requires that both be known completely. This view is commonly applied to games of chance like coin flipping, dice rolling, card selection and lottery playing. The probability of an event (e.g. coin - 0.5 probability of heads, dice - 1/6 probability of a one, cards - 1/13 chance of selecting an ace from a full deck) can be predicted strictly from an analysis of a set of circumstances. More complicated outcomes can then be calculated without actually performing the action, using the mathematical laws of permutations and combinations.

The frequency school establishes probability based on observations of repeated events or trials. This view is used in actuarial work (e.g. insurance - based on prior outcomes). The difficulty with the frequency view is that it only applies well to stable and repetitive processes. The advantage of this approach is that it can be applied to any situation which can be observed through many repetitions, including those cases amenable to classical analysis. Unfortunately many events cannot be measured this way simply because they are rare or cannot be repeated a sufficient numbers of times to extract relative frequency.

The subjective school holds that probability is not a strictly objective value, rather probability estimates reflect a degree of belief. The source of the uncertainty is limited knowledge based on experience. There is uncertainty at many levels . A probability value itself creates uncertainty for any future observations because unless the probability is = 1, you are uncertain which outcome will happen, only how likely a given outcome may be. But you are also subjective to uncertainty in the probability estimate. You can be highly

certain that the probability of rolling a six with a single die is 1 in 6, IF the die is fair, but you can be much less certain that your probability of getting colon cancer from drinking chlorinated water is 'x'. The advantage of this view is that it is much more flexible than the frequency school and allows the probability to change over time and to have competing views of the probability. Both classical and frequency schools are unable to support assessed risk prediction. That is why the subjective school is widely adopted for dealing with uncertainty in risk analysis (Morgan et al., 1990).

1.3.2.2 Uncertainty

Similar to probability, uncertainty can be defined several different ways. For the purpose of this thesis, uncertainty will be considered to consist of two parts: variability and lack of knowledge. This distinction was highlighted by Hoffman and Hammonds (1994) who also referred to it as Type A and Type B uncertainty.

Before explaining uncertainty due to lack of knowledge and uncertainty due to variability it is useful to point out that some things do not contain any uncertainty. These include statements made from the classical view of probability. Always assuming something is fair, statements like there is a 0.25 probability that if you flip two coins two tails will be face up (while there is no uncertainty in the probability, uncertainty still exists in the outcome of actual coin tosses). Other numbers that do not contain uncertainty relate to things that can be counted thoroughly or discrete numbers. Examples include the number of brothers you have, your age in years, the date you received your first drivers license, how much money you are now carrying. These statements are objective, they need not contain any uncertainty if they are known accurately. Unfortunately, most health risk information contains uncertainty, either due to lack of knowledge or inherent variability.

Uncertainty due to lack of knowledge is usually the largest source of uncertainty. Finkel (1990) identified three areas that could fall under lack of knowledge in his focus on risk assessment issues. Parameter uncertainty (includes measurement errors, random errors systematic errors), model uncertainty (very important for predictive information) and decision-rule uncertainty (associated with value judgments - also important for predictive information).

Uncertainty due to variability occurs when a single number is used to describe something which has multiple values. Variability is often discounted by using values based on the mean of all values occurring in a group. A common assumption for health risks has been that everyone has the same susceptibility to a particular risk factor when in reality large inter-individual variations do exist. Similarly mean values are often used for estimating exposure to a group when large variations in exposure actually occur. A second type of variability arises when a single value does exist but it changes constantly over time. The population of Canada is a single value at any instant but it varies daily (note: most of the uncertainty in the population is due to lack of knowledge, the difficulty of measuring the population accurately on any day).

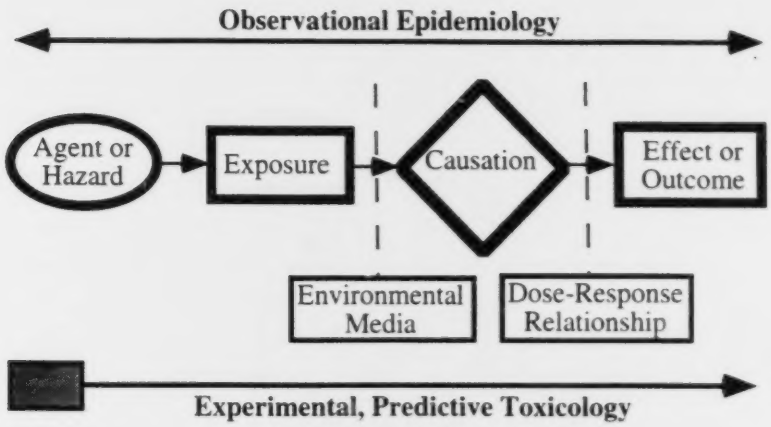
Figure 1.2 shows the causal chain model linking an agent or hazard to the effect or outcome. Different levels of uncertainty in health risk estimates occur at each step in the model. This thesis only focuses on the uncertainty in health risk estimates associated with the effect or outcome. A different characterization of levels of uncertainty would occur if other steps in the model were analyzed.

Figure 1.2 Causal Chain Model for Environmental Health Risks

Figure 1.3 attempts to depict the relationships of our knowledge on health risks by contrasting what is known with certainty with the relative uncertainty faced in most cases. Knowledge is gained about any issue by collecting information which, if relevant to the issue, may be considered to constitute evidence on that issue. In most aspects of knowledge, evidence alone cannot define our knowledge, and logic and inference must be used to interpret evidence to establish knowledge. All knowledge involves varying degrees of evidence and inference which is shown in the hierarchy of uncertainty for health risks. At the base, direct evidence requires limited inference and the corresponding uncertainty is low. Moving up the figure involves greater reliance of inference to compensate for the shortage of evidence. In the middle both evidence and inference are used to supply knowledge. Near the top the uncertainty in the knowledge increases to the point where the certain knowledge may become only a tiny fraction of our knowledge in relation to a much larger proportion of uncertainty. At the top where we have no evidence, only inference, the uncertainty is enormous.

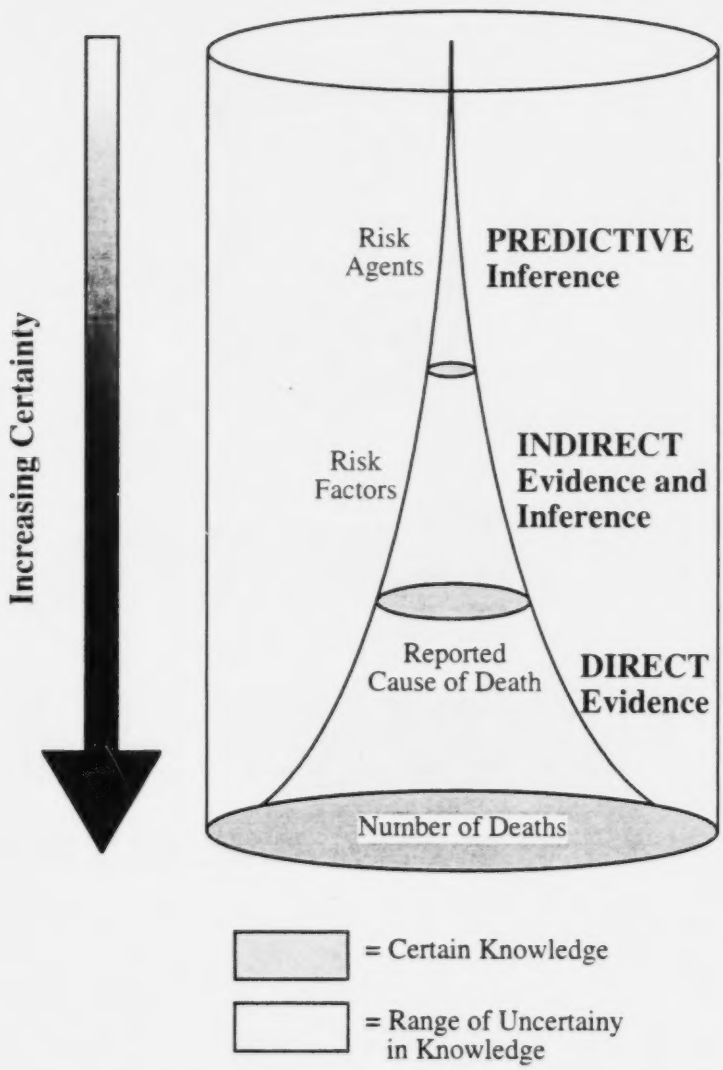
Figure 1.3 Health Risk Evidence, Inference and Uncertainty Hierarchy

Figure 1.2 Causal Chain Model for Environmental Health Risks



Adapted from Hrudey, 1996b, Figure 1

Figure 1.3 Health Risk Evidence, Inference and the Uncertainty Hierarchy for Adverse Outcomes



1.3.3 Risk Perception

The term risk perception almost inherently establishes a dichotomy between quantitative risk predictions and levels of perceived risk. If people think a risk probability is larger or smaller than a quantitative risk prediction then it is because of how they perceive it. Much work on risk perception originated with various technological risks arising from energy production and in particular nuclear power (e.g. Rasmussen, 1981). Even though the numerical estimates of the annual risk from nuclear power have been reported to be much smaller than most common health risks, many people regard nuclear power as representing an unacceptably high health risk. Risk perception research has sought to identify factors which can explain these differences.

A problem arises when anyone presumes that a numerical probability estimate can be considered to be the "real" risk. This leads to a conclusion such as those who fear a risk with a low probability are "irrational". Such conclusions ignore the multiple dimensions of risk, other than probability and they stretch the meaning of "real" by assigning this to anyone's estimate of the risk probability.

This thesis presents numerical information which could be used unwisely to dismiss peoples concerns about specific health risks. The numerical values in this report are an attempt to summarize the most reliable information about health risks but these numbers are not presented as being the "real" risks (probabilities). Many valid non-numerical or qualitative factors do affect how important any particular health risk will be to any individual. For example, prolonged painful death is not the same as sudden, painless death, yet death statistics do not distinguish such differences with probability estimates.

What this thesis does propose is that people should consider the available numerical values and understand how this information was generated so they may consider uncertainties in developing their own perception of risk. The following are some of the factors that are known to influence individual perceptions of the risk.

1.3.3.1 Framing

Framing is often used to explain why people underestimate large risk probabilities and overestimate smaller ones. Slovic et al. (1979) have performed several surveys highlighting this phenomena. The framing explanation for this is that people grow accustomed to the more common causes of death. The media plays a large role in this. Except for the obituary pages in the newspaper, the number of people dying from cardiovascular disease, cancer or other chronic diseases is not routinely reported. Even car accidents, which are often reported, receive only little media attention unless there were special circumstances surrounding the event (e.g. multiple deaths, famous person, etc.). However, whenever there is a plane crash or an increase in a rare diseases (e.g. hantavirus scare in 1995) extensive media coverage is devoted to these topics. A more direct example of framing is the different perception attached to expressing risk as a 99% chance of survival rather than as a 1% chance of death.

1.3.3.2 Personal vs. External

This distinction is commonly referred to as voluntary versus involuntary risks. Again studies have consistently shown that people are less concerned about risks that they have a choice about rather than those that are imposed on them without choice. A lot has to do with the benefit people derive from an activity. People gain a lot of personal benefit from operating a motor vehicle but may see less benefit from a factory at the edge of town.

Similar to voluntary and involuntary are whether the risk is controllable or not (e.g. water vs. air pollution) and the potential harm if something does go wrong. A classic example here is the nuclear industry, where the annual risk of harm to the public is predicted to be very low while the threat of harm is perceived as very large.

1.3.3.3 Immediate vs. Delayed

Many are less concerned about future harm than present harm. Most deaths are not immediate (i.e. a few minutes or hours) but involve a slow degenerative process. There are two important exceptions to this, heart attacks and fatal injuries. Over 10% of deaths in Canada are from acute heart attacks (acute myocardial infarction). Fatal injuries (external causes of death) accounted for 7% of deaths in Canada and includes suicides, motor vehicle accidents, falls and poisonings.

1.3.3.4 Characteristics

Certain disease are more feared than others because of pain involved or how debilitating they are such as cancer or Alzheimer's.

1.4 Literature Review

1.4.1 Popular Literature

The term popular books refers to books that have been specifically written and marketed for the general public versus academics or some other group of professionals. The popular books were rarely used in my thesis and in most cases served to highlight the difficulty of presenting health risk information in an accessible, understandable and accurate way.

Living with Risk by the British Medical Association (1987)

This book has a very similar purpose to this thesis and is one of the best books at presenting information in an accurate way while keeping it suitable for the public. The main causes of death are reviewed as well as some of the major risk factors including chapters on occupational, transportation, recreational and chemical risks. Information on the nature of risk and on the perception of risk is included. However, the distinctions of the evidentiary basis and uncertainty associated with the source of the risk information is not extensively developed. Likewise, the health risk data is for the United Kingdom prior to 1985.

The Book of Risks by L. Laudan (1994)

This book, subtitled "Fascinating Facts About the Chances We Take Every Day" includes chapters on risks of accidents, travel, health, crime, sin, nature & technology. Numerous figures and tables are used but most of the book consists of single line statements of a risk followed by a probability estimate. While the goal of this book is similar to Living with Risk and this thesis, to help people understand risk, the book makes many ill-concerned comparisons which misinform. Statements like "If you keep a pet bird at home, you are 500 percent more likely to get lung cancer than you are from exposure to second hand smoke" (pg. 19) are used by the author to support his own personal perspective. The book does not address uncertainty nor describe the different sources of information and it is not clear that the author is aware of any of the differences.

Beating Murphy's Law by B. Berger (1994)

This book takes a different approach than the "The Book of Risks" to present information about everyday risks. The numbers are embedded within a fictionalized, often humorous story to provide some context for the risks and this allows the author to explain many of the cautions required when interpreting the risk values. However, this book also does not address the issue of uncertainty. Probabilities of flipping coins are given the same certainty as the odds of developing cancer from eating peanut butter every day of your life.

Risk Watch by J. Urquhart and K. Heilmann (1984)

This older book written by two doctors is a more academic book on risk in that it goes into much more detail. The book starts out by tracing the decline in mortality in the twentieth century and describes the major causes of death. This is followed by information on prominent voluntary hazards, medical and surgical and food risks. One of the innovations of the book is a log scale they propose to use for comparing risks.

1.4.1.1 Information from Health Agencies

Health agencies exist for all the major diseases and many of the minor ones that supply information to the public as brochures or booklets about the risk from the particular disease. This information usually describes what the disease is, how common it is and what if any preventive actions can be taken to reduce the risk. This information was mainly used to check that any important information (e.g. risk factors) were included since they rarely contained quantitative data which can be referenced. Two particularly useful annual publications which do contain quantitative information are the Canadian Cancer Statistics and Heart Disease and Stroke in Canada.

1.4.2 Textbooks

Textbooks provided some of the most relevant information for this thesis because they often summarize the most important information that is available.

Mortality, Morbidity and Health Statistics by Michael Alderson (1988)

This book was one of the main references for the section on direct information especially relating to the uncertainties involved.

Public Health and Preventive Medicine in Canada by C.P. Shah (1994)

Provides on overview of health in Canada from a public health perspective. This source was used to identify and describe several of the risk factors.

Casarett and Doull's Toxicology edited by M.O. Amdur, J. Doull and C.D. Klaassen (1991)

One of the best known introductory texts on toxicology. This source was used for the predictive section and for some of the environmental risk factors in the indirect section.

1.4.3 Scientific Journal Articles

Journal articles comprise the majority of current information available on health risk. However only articles of a summary or more general nature were useful for this thesis. Most of the risk factors addressed in the indirect section could each fill a book just by reviewing the available literature. Some of the articles which were used came from important medical journals in addition to journals like Risk Analysis and Science. Two important Canadian medical journals are the Canadian Journal of Public Health and the Canadian Medical Association Journal. Two specific journal articles were particularly useful:

The Causes of Cancer: Quantitative Estimates of Avoidable Risks of Cancer in the United States Today by R. Doll and R. Peto (1981)

This remains the most widely recognized summary of the risk factors associated with cancer. They used epidemiological information to develop estimates of the major causes of cancer and they included ranges to identify the uncertainty associated with their estimates.

Estimating Cancer Mortality by Michael Gough (1989)

This article established a link between some of the estimates from the Doll and Peto (1981) study based on epidemiology and estimates from the U.S. EPA based on toxicological risk assessment.

1.4.4 Government Publications

Government publications are often the best source for Canadian specific information. Most of the information in the direct information section is from government publications and many of the Canadian references in the other sections are from government publications.

Statistics Canada

An enormous volume of information is published annually by Statistics Canada on all aspects of Canada. For this thesis, the annual publications on mortality served as data for most of the figures and tables in the direct information section. Information on population and occupational information was taken from additional publications. A quarterly publication entitled Health Reports supplied several articles used in the thesis in both the direct and indirect information sections.

Health Canada

Several key articles used in this thesis from Health Canada were on health risk determination and carcinogen assessment. The Canadian Environmental Protection Act documents published by Environment Canada supplied the exposure information for the predictive information section results (The U.S. EPA provided potency values from their IRIS database). Health Canada also publishes the bimonthly Chronic Diseases in Canada.

Transport Canada

Transport Canada publishes annual documents which summarize motor vehicle injuries and fatalities. A document on motor vehicle use and alcohol consumption was also used.

1.5 Perspective About Numbers

1.5.1 Log vs. Normal Scale

People usually work with numbers that range within a couple orders of magnitude (e.g. percentages ranging from 1-100%). However, when dealing with health risks the differences can easily range eight order of magnitude or more. For this reason log scales must often be used in figures. Figure 1.4 (log scale) and 1.5 (normal scale) will be used highlight the importance of using log scales and some of the difficulties in interpreting them. The same eight values are shown in both figures numbers (0.5; 1; 50; 100; 5,000; 10,000; 500,000 and 1,000,000). Both figures have a similar range on the vertical axis except 0.1 was used for the log scale since it cannot have a zero.

Figure 1.4 Log Scale Example
Figure 1.5 Normal Scale Example

The need for using log scales to show all the numbers is clearly demonstrated with these figures. All eight values are clearly shown on the log scale while only four are shown (and two just barely) on the normal scale.

Since log scales are used extensively in the direct information section of this thesis a few points and cautions need to be mentioned for those unfamiliar with their interpretation:

- all values are proportional to each other. For example, in Figure 1.3 the vertical distance between points 1 - 2, 3 - 4, 5 - 6 and 7 - 8, which are all twice as large/small than each other are the same. Likewise points 1 - 3, 2 - 4, 5 - 7 and 6 - 8 are all ten times as large /small and have the same vertical distance between them.
- reading values off the log figures must be done with caution when they are not on a line. For example, in Figure 1.3 point 1 with a value of 0.5 appears to be closer to one than it is.
- log scales appear to over-emphasize low values. For example, in Figure 1.3 it would not be possible to recognize that point 2 is one million times smaller than point 8 without looking at the scale (a similar bar on the normal scale would be just over ten times smaller).

Figure 1.4 Log Scale Example

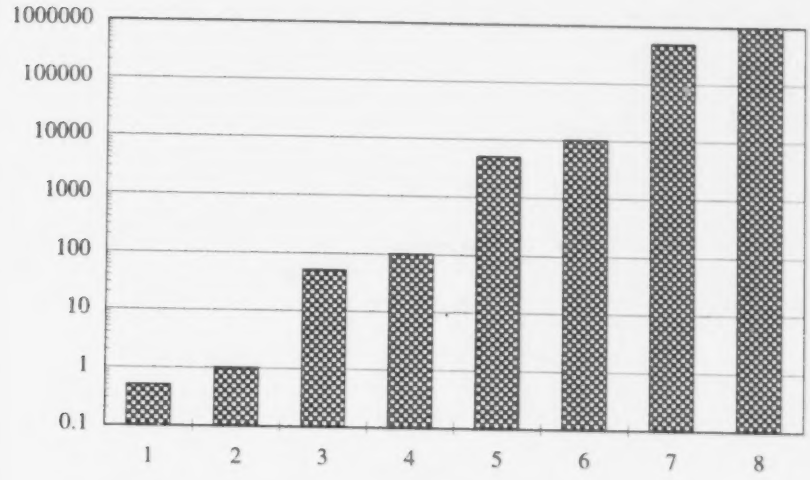
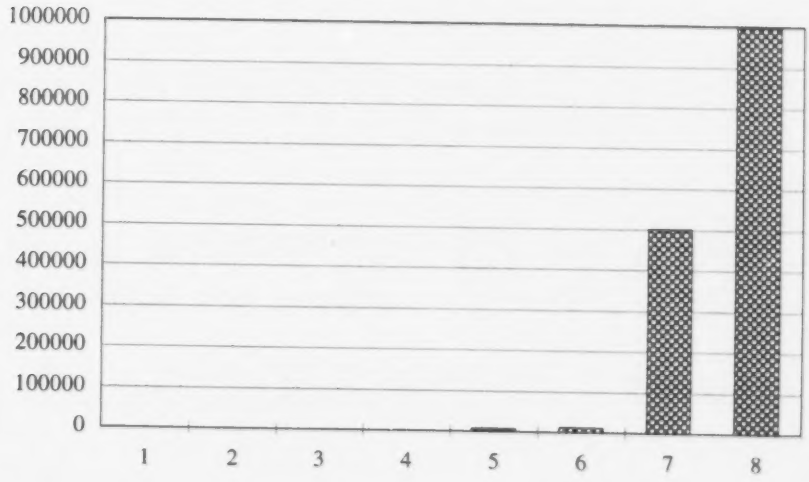


Figure 1.5 Normal Scale Example



- log scales appear to minimize differences. For example point 7 on the normal scale is clearly one half of point 8 while on the log scale they appear to be similar.

Apart from noticing the axis number are increasing proportionately, all log scale figures in this thesis include tick marks beside the axis.

1.5.2 Annual vs. Lifetime

A time must be included with a risk estimate. For health risks, annual or lifetime risks are usually used. Direct information is usually expressed on an annual basis since the information is collected and summarized annually. However, predictive information is expressed as the lifetime probability of developing cancer. Knowing which time frame is being used is important since the risk estimate may be 70 times (the standard age used in toxicological risk assessment) higher or lower.

1.5.3 Categories

A potential problem with presenting numbers is that it is fairly easy to manipulate them to suit ones own purpose. This can be done be choosing categories that emphasize or de-emphasize the health risk you are concerned with. A couple ways to do this are:

- to make one category seem larger than others you can sub-divide all the other categories into smaller ones, making yours stand out more. For example to emphasize cardiovascular disease compared with cancer, cardiovascular disease could be divided into two categories (heart disease and stroke) while cancer could be divided into several (lung, colorectal, breast, prostate, bladder, ...).
- since health risks vary tremendously with age, selecting a specific age range can highlight a particular factor. A leading cause of death in a specific age range (e.g. early in life) may account for less than 1% of deaths overall.

While these methods are valid when it is clearly shown what has been done, they can confuse people because there appears to be several different 'leading' causes of death.

1.5.4 Totals and Change

To emphasize a health risk the can be selectively shown as a relative change or as the total increase. There are two scenarios:

- small total increase, large relative change. For example, if the annual number of deaths from a cause increased from 2 to 20 (an increase of 18 deaths), you can state 'the number of deaths from the cause increased by a factor of 10' (or to add even more emphasis 1000%).
- large total increase, small relative change. For example, if the annual number of deaths from a cause increased from 50,000 to 51,000 (a 2% increase) you can state '1,000 more deaths from the cause this year'.

The best method is to include the numbers (e.g. 2 to 20; 50,000 to 51,000) with any statement .

1.5.5 Rare Events

Rare events happen all the time. However, there is a big difference between predicting the occurrence of rare event (e.g. this ticket winning the lottery) versus looking at all occurrences and identifying a rare event (e.g. any ticket winning the lottery). Another example is predicting what blade of grass a properly hit golf ball will come to rest on in the fairway. The probability that it will land on any specific blade of grass is incredibly small (i.e. 1 in many millions), the probability that it will land on any blade of grass is one (i.e. 1 in 1). Similarly, it is hard to predict who will die from a rare event but with approximately 200,000 annual deaths in Canada, it is very likely there will be rare deaths (e.g. killed by lighting - approximately 1 in 40,000 annual risk, see discussion).

In conclusion, health risk information must be interpreted with caution. The media, owing to interest expressed by the public, has taken it upon themselves to identify all the risks that are out there. Every day new risks are identified, often in things that were once thought to be safe. Often reports contradict one another leaving people confused about what the risks are. Some of these contradictions relate to how the numbers are expressed, others to tangible differences in the information. All this information seems to lead to an almost undeniable fact, "everything involves risk". Even not doing something involves a risk, lying in bed involves risk (many people die in their beds), eating, breathing, walking, driving all involves varies amounts of risk. However, the most important question is not whether there is a risk - but how large is the probability of the risk?

2. DIRECT EVIDENCE

Evidence on death is one component of the larger field of information called vital statistics. Vital statistical information on death is generated from the death registration form that is filled out for each death. All direct evidence is based upon information taken and summarized from the individual death registration forms. The death registration form provides six pieces of information on the deceased that are commonly collected and summarized: the death itself, the sex, the age, the marital status, the usual residence and the cause of death. The cause of death stands out as one of the most valuable pieces of evidence; able to answer the question - what do we die of? Unfortunately, the cause of death is also the most difficult and uncertain pieces of evidence, as will be highlighted throughout this section and summarized at the end.

After describing the relevant parts of the death registration form in detail, information is provided on the use of rates and age standardization. Following this, information for Canada for each of the six pieces of information listed above are provided. A detailed amount information is presented for the latest available year, 1993, followed by trend information for 1930-1990. As will become evident, direct evidence provides a large and valuable resource of mortality evidence for Canadians.

2.1 Vital Statistics

Vital statistics summarize information that relates to human life. The primary vital statistics are births, deaths and marriages. Stillbirths, abortions and adoptions may also be included. Table 2.1 is a summary of vital statistics for 1993 (the latest year with information available on mortality).

Table 2.1 Vital Statistics, 1993

For the past several years, including 1993, there have been approximately twice as many births as deaths in Canada. An interesting coincidence is that a similar ratio exists between marriages and divorces.

Historical recording of vital statistics began in Canada in the early 1600's when the church in Quebec began registering the information. However, it was not until 1921 that an annual publication combining vital statistics nationally for the other eight Canadian provinces started. Quebec was added in 1926, Newfoundland joined in 1949 when it joined confederation and information for the Territories was combined starting in 1956 (Statistics Canada, 1995a).

Statistics Canada, the successor to the Dominion Bureau of Statistics produces annual publications on vital statistics in addition to numerous other statistical data reports. These annual publications, and particularly those relating to mortality, have been used to generate the majority of the evidence presented in this section. This evidence is the cumulative result of the experience of recording vital statistics that began hundreds of years ago.

Table 2.1 Vital Statistics, 1993

Vital Statistic	Male	Female	Both
Live Births	199,744	188,650	388,394
Deaths	109,407	95,505	204,912
Marriages	-	-	159,316
Divorces	-	-	78,226

Data Source: Statistics Canada, 1996 and Colombo, 1995

2.2 Death Registration Form

A death registration form is filled in for every known death in Canada. Figure 2.1 is a copy of the standard death registration form designed and printed by Statistics Canada for use by provinces and territories. A province may use its own form as long as it includes the same standard information. The death registration form supplies information that is the most 'direct' link to mortality. For this reason it is important to understand the process relating to, and the contents, of the death registration form.

Figure 2.1 Death Registration Form

2.2.1 Process

The process of registering a death is as follows:

> "The form for the registration of death consists of two parts, personal and medical. Personal data are supplied by an informant, usually a relative of the deceased. The informant signs this part of the certificate and is responsible for delivering the form to the undertaker. The part of the form comprising the medical certificate of death is completed by the medical practitioner last in attendance or by a coroner, if an inquest or enquiry was held. The undertaker, or person acting as the undertaker, enters details on burial or their disposition of the body on the death registration form. He is also responsible for filing the completed form with the local registrar who then issues the burial permit." (Statistics Canada, 1995a, pg. ix)

In the death registration form (Figure 2.1), the informant fills in sections 1 - 19, the medical practitioner or coroner fills in sections 20 - 30 and the undertaker fills in sections 31 - 34.

2.2.2 Contents

While many parts of all death registration forms are ultimately compiled by Statistics Canada there are five sections of particular relevance to direct evidence. In addition to the form itself, these five sections are listed in Table 2.2 with the related section from the death registration form (Figure 2.1).

Table 2.2 Death Registration Form Sections Related to Direct Evidence

Figure 2.1 Death Registration Form

MODEL (1971)

Province of (Canada)

Registration of DEATH

Registration No.(Department Use Only)

(Do not write above this line)

NAME OF DECEASED
1. Surname of deceased (print or type) — Social Insurance Number
All given names — 2. Sex

PLACE OF DEATH
3. Name of hospital or institution (otherwise full address where death occurred) — City, town or other place (by name) — Inside municipal limits? (state Yes or No) — County or district

USUAL RESIDENCE
4. Complete street address if rural give exact location (not PO or RR address) — City, town or other place (by name) — Inside municipal limits? (state Yes or No) — County or district — Province (or country)

MARITAL STATUS
5. Single, married, widowed or divorced (specify)
6. If married, widowed or divorced, give full name of husband or maiden name of wife

OCCUPATION
7. Kind of work done during most of working life
8. Kind of business or industry in which worked

BIRTHDATE
9. Month (by name), day, year of birth

AGE
10. Years If under(Months)(Days) If under(Hrs.)(Min.)
1 year — 1 day

BIRTHPLACE
11. City or place, province (or country) of birth

This space reserved for optional item(s)

FATHER
12. Surname of father (print or type)
All given names
13. City or place, province (or country) of birth - father

MOTHER
14. Maiden surname of mother (print or type)
All given names
15. City or place, province (or country) of birth - mother

SIGNATURE OF INFORMANT
16. Signature of informant — X
17. Relationship to deceased
18. Date signed: Month(by name), day, year
19. Address of informant

MEDICAL CERTIFICATE OF DEATH

20. DATE OF DEATH: Month (by name), day, year — Approx. interval between onset and death

21. CAUSE OF DEATH
Part I
Immediate cause of death (a) — due to (or as a consequence of)
Antecedent causes, if any, giving rise to the immediate cause (a) above, stating the underlying cause last (b) — due to (or as a consequence of)
(c)
Part II
Other significant conditions contributing to death but not immediate cause (a) above

22. Autopsy Yes No — being held? ☐ ☐
23. Does the cause of death stated above take account of autopsy findings? Yes ☐ No ☐
24. May further information relating to the cause of death be available later? Yes ☐ No ☐
25. If accident, suicide, homicide or undetermined (specify)
26. Place of injury (e.g. home, farm, highway, etc.)
27. How did injury occur? (describe circumstances)
28. I certify that the above named person died on the date and from the causes stated herein: Signature: X
29. Designation: Attending physician ☐ Coroner ☐ Other ☐ Date certified: Month (by name), day, year
30. Name of physician or coroner (print or type) Address:

DISPOSITION
31. Burial, cremation or other disposition (specify)
32. Date of burial or disposition: Month (by name), day, year
33. Name and address of cemetery, crematorium or place of disposition

FUNERAL DIRECTOR
34. Name and address of funeral director (or person in charge of remains) (print or type)

For (Department Use Only)

CERTIFICATION OF (DIVISION) REGISTRAR
I certify this return was accepted by me on this date:
Signature of (Division) Registrar Date: Month (by name), day, year
This space reserved for optional item(s)

Statistics Canada, 1995a, Appendix 1

Table 2.2 Death Registration Form Sections Related to Direct Evidence

Name	Related Section on Death Registration Form	Related Section in Thesis
Registered Death	Entire Form	2.4
Sex	2	2.5
Age	10	2.6
Marital Status	5	2.7
Usual Residence	4	2.8
Cause of Death	21	2.9

Registered Deaths

Collectively all the death registration forms from a single year provide the annual number of deaths. This annual number is the starting point for all direct evidence statistics. Subsequent divisions of this number provide more detailed, but often less precise evidence.

Sex

Males and females often have significant differences in their mortality patterns. For this reason separate evidence is provided where possible.

Age

On the death registration form, deaths aged one and older are completed in years and deaths aged less than one are completed in months or days. Following the first few years of life, increasing age is strongly and exponentially associated with increasing mortality. In addition the age at death provides valuable insights into different causes of death.

Marital Status

The marital status of the deceased is completed as single, married, widowed or divorced. Associations between marital status and mortality occur but the reasons for the associations are uncertain.

Usual Residence

The usual residence information includes province (or territory), census division (or county) and locality (city, town or village). Similar to marital status an association with geographic residence and mortality exists but reasons are uncertain.

Cause of Death

Of all sections on the death registration form, the cause of death is most useful for understanding health risk but is the most difficult to complete accurately. Section 2.9 describes how this section is filled out and what information is used.

Other standard information that is collected and published by Statistics Canada include the residence, birthplace, birthplace of parents, date of death, province of occurrence of death, place of accident and autopsy (Statistics Canada, 1995a).

This discussion of direct mortality evidence comes from publications based on evidence collected directly from death registration forms.

2.3 Evidence Source, Population and Rates

This section provides some background information before presenting direct mortality evidence in detail and is divided into three parts. The first part, on evidence source describes what information was collected. The second part presents evidence on population which is required for generating mortality rates which are discussed in the third part. One important type of rate is the age-standardized rate which is described in more detail in Section 2.3.3.1.

2.3.1 Evidence Source

Most of the information in this section is generated from vital statistics published by Statistics Canada and its predecessor the Dominion Bureau of Statistics. For many of the sections the evidence was been divided in two parts: 1993 information and trend information from 1930-1990.

For detailed analysis, 1993 was chosen because it was the latest available year for mortality evidence. While some types of evidence like population estimates are more current, they are of little use when the focus is on mortality. Since most aspects of mortality vary gradually from year to year, current mortality levels are similar to those in 1993.

Changes in most aspects of mortality from year to year in Canada have been relatively small. However, cumulatively over the last 60 years some significant changes have occurred. One of the main advantages of direct evidence is its comparability over time (and place) which helps highlight cumulative changes. For this reason, trend evidence from 1930 - 1990 has been included in this analysis. 1930 was chosen even though compilation of vital statistics from different provinces began in 1921. Quebec which accounts for a significant portion of Canadian mortality was not included until 1926, so for convenience the trend evidence was started in 1930. Even though Newfoundland and the Territories were added later they had less effect on Canadian mortality statistics.

To keep the amount of data within manageable proportions, evidence for this analysis was collected in five year increments. This supplied enough evidence to plot the trends for basic mortality statistics and major causes of death. Often similar types of trend evidence are presented by Statistics Canada but with five year increments ending with years 1 and 6. the census years. However, the census itself has no bearing on the quality of the annual mortality statistics.

Table 2.3 presents what evidence was included for 1993 and Table 2.4 for 1930-1990.

Table 2.3 1993 Evidence

Table 2.4 1930-1990 Trend Evidence

Evidence by sex is presented for males and females separately in most cases. When the sexes were combined the data are labeled 'both'.

Age evidence is divided into five year increments except for the first two and last age categories. Recognizing the large difference in mortality between the first year of life and those immediately following, the first five year increment is divided into 0 - 1 and 1 - 4 categories. The upperbound for the age was determined by the available information. For 1993 this was 90+. While much of the trend evidence included age categories until 100+, some contained only 85+ which ended up being the limiting upper age category. Changing the last age category for 1993 to 85+ would have allowed for better comparison with trend evidence, however a large number of people currently live beyond 85 so providing an extra age category provides useful evidence.

For marital status 1993 evidence was not readily available and 1990 evidence was used instead. For usual residence information, 1993 evidence was divided by province.

Detailed cause of death evidence is presented for 1993. This includes detailed breakdowns of all causes of death by major category and by age categories. For trend evidence five major causes of death were selected for presentation. Currently, four of these five are the leading causes of death (based on the percentage of total deaths) while the fifth, infectious diseases, was a leading cause of death earlier in the century.

2.3.2 Population

The population is used for calculating many mortality statistics later in this thesis so population information will be presented now. The two main types of population estimates are the annual total population and the annual population subdivided by 5-year age category.

Table 2.3 1993 Evidence

Category	Divisions	Division Names
Year	1	1993
Sex	2	Male, Female
Age	19	<1, 1-4, 5-9, 10-14, 15-19, 20-24, 25-29, 30-34, 35-39, 40-44, 45-49, 50-54, 55-59, 60-64, 65-69, 70-74, 75-79, 80-84, 85-89, 90+
Marital Status	3	Single, Married, Divorced/Widowed (1990 used)
Usual Residence	12	Nfld, P.E.I., N.S., N.B., Que., Ont., Man., Sask., Alb., B.C., Yukon, N.W.T.
Cause of Death	6	Infectious, Cancer, Cardiovascular, Respiratory, External, Other
	17	17 Major Categories (see Table 2.12)
	Many	see Appendix 1 and 2

Data Source: Statistics Canada, 1995a

Table 2.4 1930-1990 Trend Evidence

Category	Divisions	Division Names
Year	13	1930, 1935, 1940, 1945, 1950, 1955, 1960, 1965, 1970, 1975, 1980, 1985, 1990
Sex	2	Male, Female
Age	19	<1, 1-4, 5-9, 10-14, 15-19, 20-24, 25-29, 30-34, 35-39, 40-44, 45-49, 50-54, 55-59, 60-64, 65-69, 70-74, 75-79, 80-84, 85+
Cause of Death	6	Infectious, Cancer, Cardiovascular, Respiratory, External, Other

Data Source:
Dominion Bureau of Statistics (1933, 1937, 1942, 1948, 1953, 1956, 1962, 1967, 1968)
Statistics Canada (1970, 1972, 1975, 1978, 1980, 1983, 1985, 1987, 1990, 1994b)

2.3.2.1 1993 Evidence

The population estimate for Canada in 1993 was 28,940,597 which included 14,343,108 males and 14,597,489 females (Statistics Canada, 1995a). At current rates it appears the population of Canada will reach 30 million in 1996 (Statistics Canada, 1995c). It should be noted that despite the apparent precision of these number (to the nearest person) these numbers are actually always estimates because the true population is changing daily and is never known exactly. Clearly it would be impossible to conduct an accurate count of every Canadian on any given day. Section 2.3.2.3 discusses population uncertainty.

Table 2.5 Population by Age Categories, 1993

2.3.2.2 Trend Evidence

Population separated by sex are summarized for the years 1930-1990.

Figure 2.2 Population, 1930-1990

Figure 2.2 shows the Canadian population between 1930 and 1990 for males, females and both combined. The population has increased 2.6 times between 1930 (10.2 million) and 1990 (26.6 million). There was a greater number of males in 1930 (8% greater) which disappeared by the 1970's and by 1990 there was a greater number of females (3% greater). From 1970 to 1990 the total population has been increasing by approximately one million every four years.

Because the number of people dying in a year is related to the number of people living, the annual population must be used to calculate rates (number of deaths per unit population) allow for comparison between years. Rates are discussed in Section 2.3.3.

When analyzing mortality by age category, the matching population estimates are required as well. Similar information to Table 2.5 was collected for each fifth year between 1930-1990 except one less age category was used (no 90+). In addition to the total number of people in each category, the relative number of people between categories is important as well. To show these number of people on a relative basis, population pyramids or population age distributions are used.

Figure 2.3 Population Age Distributions, 1930, 1950, 1970 and 1990

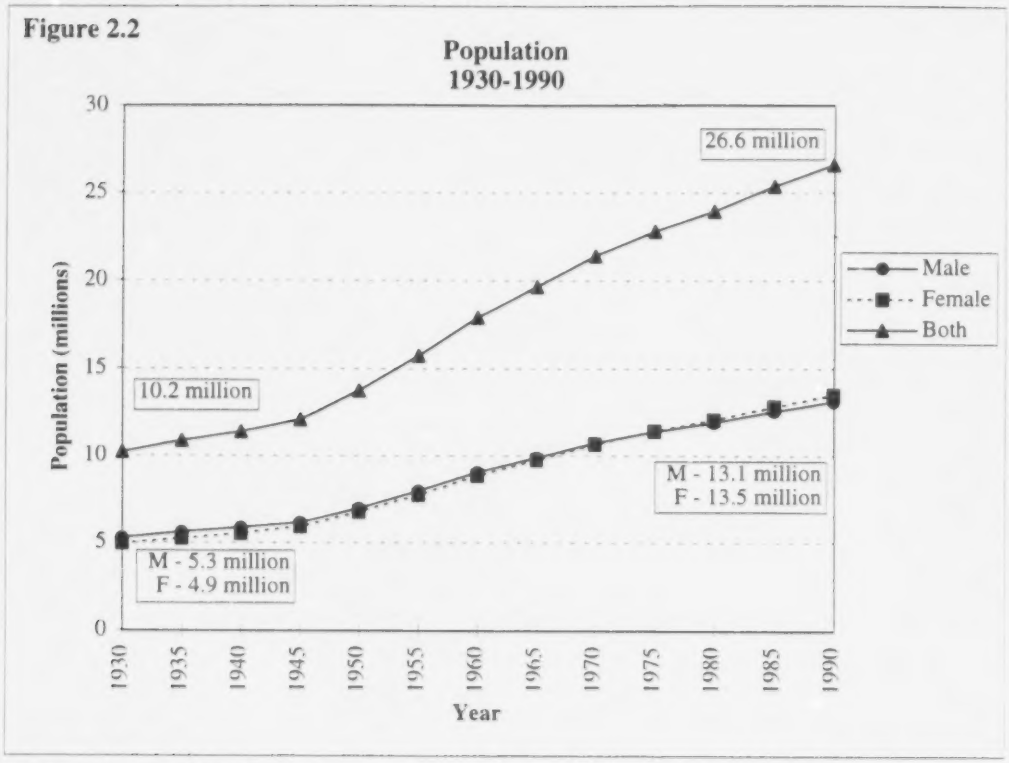
Figure 2.3 shows the male and female age distributions for 1930, 1950, 1970 and 1990. The lines represent the percentage of the total male and female population found in each 5

Table 2.5 Population by Age Categories, 1993

Age Categories	Males	Females	Both
<1	199,744	188,650	388,394
1-4	826,409	788,023	1,614,432
5-9	1,003,285	962,731	1,966,016
10-14	1,005,225	957,682	1,962,907
15-19	995,304	949,613	1,944,917
20-24	1,058,505	1,029,613	2,088,118
25-29	1,211,202	1,181,079	2,392,281
30-34	1,354,413	1,320,181	2,674,594
35-39	1,253,714	1,243,675	2,497,389
40-44	1,105,090	1,098,607	2,203,697
45-49	956,962	942,496	1,899,458
50-54	732,813	727,440	1,460,253
55-59	620,358	624,879	1,245,237
60-64	593,880	618,573	1,212,453
65-69	512,630	589,451	1,102,081
70-74	400,152	515,188	915,340
75-79	262,252	378,726	640,978
80-84	155,905	261,636	417,541
85-89	67,170	142,419	209,589
90+	28,095	76,827	104,922
Total	14,343,108	14,597,489	28,940,597

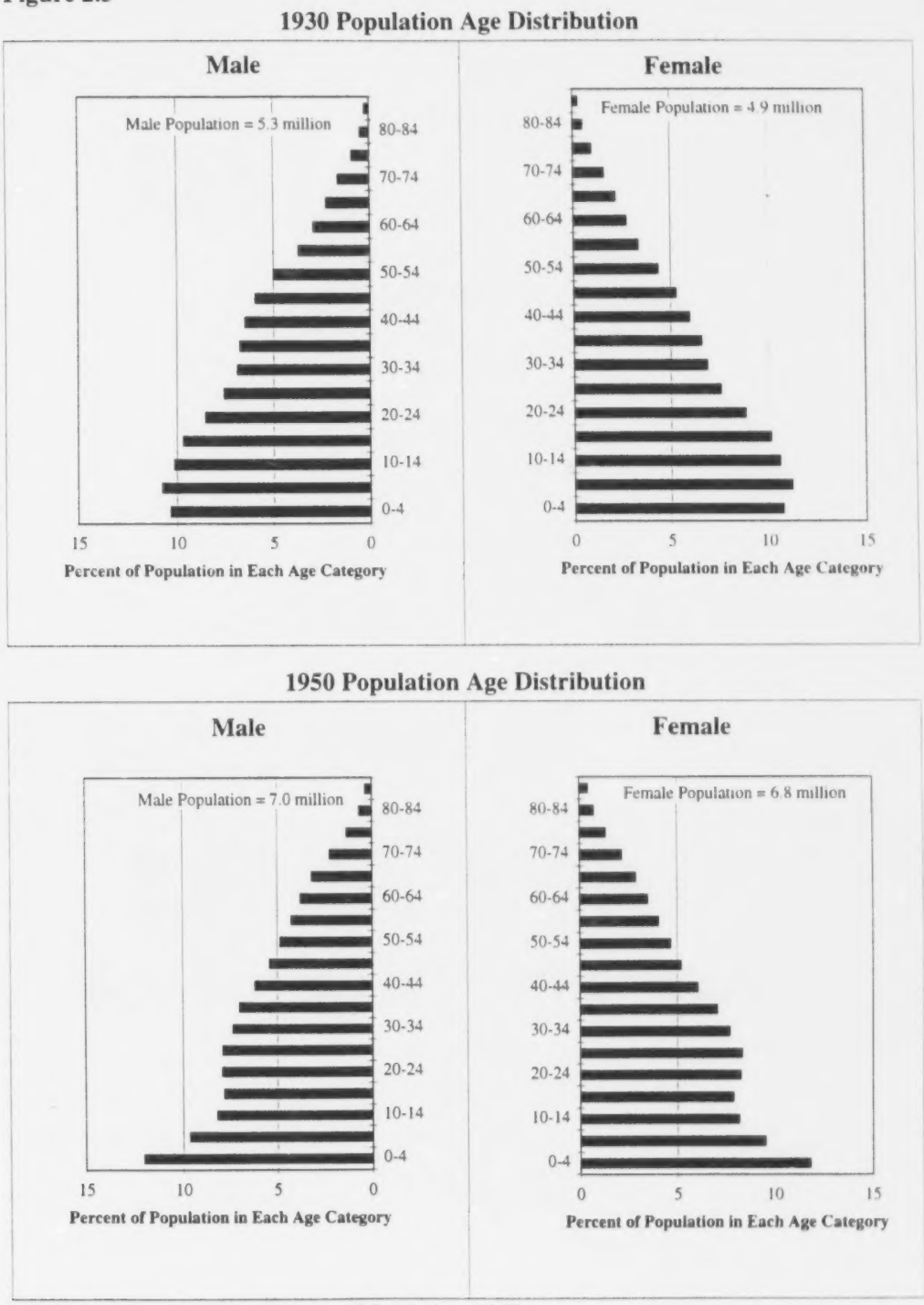
Data Source: Statistics, 1995a, Appendix 2

Figure 2.2



Data source: see Table 2.4

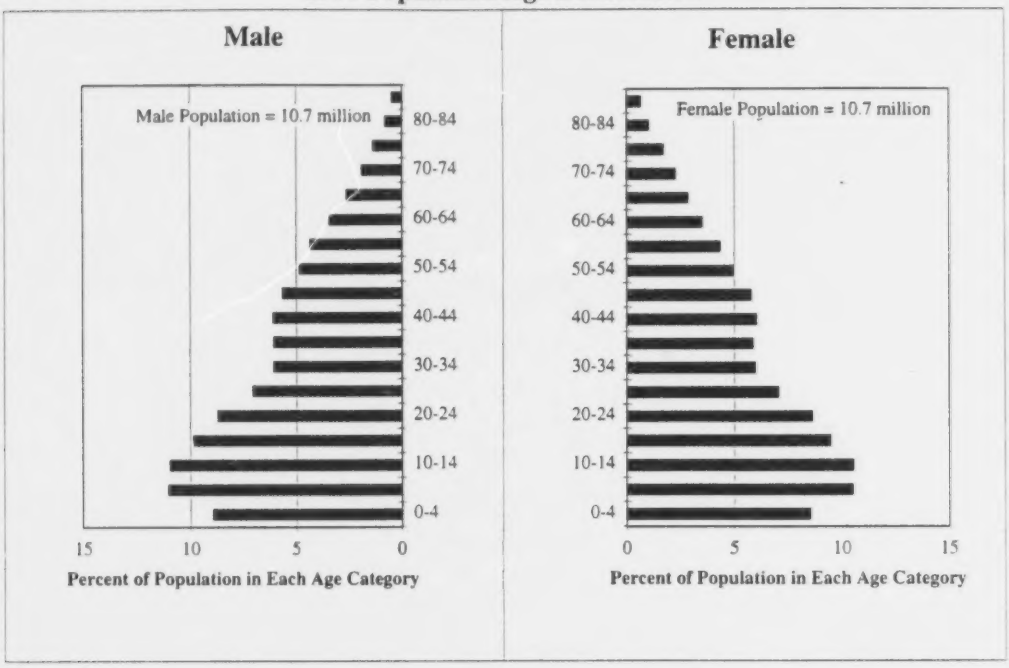
Figure 2.3



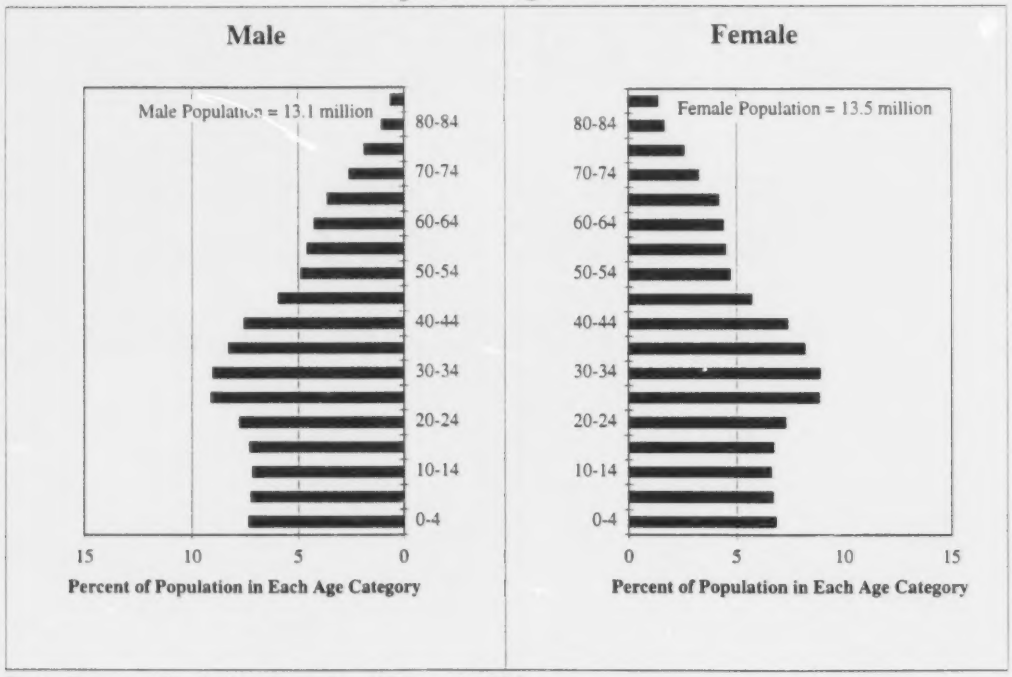
Data Source: Dominion Bureau of Statistics, 1968

Figure 2.3 (Cont'd)

1970 Population Age Distribution



1990 Population Age Distribution



Data Source: Statistics Canada, 1970 and 1990

year age category (and one 85 and greater age category). These figures illustrate what has been called the baby boom. In 1950 it is in the 0-4 and 5-9 categories, by 1970 it was in the 0-4 to 25-29 categories and by 1990 it is in the 25-29 to 40-44 categories. In addition, there has been an increase in the relative number of older people, especially females, which is indicative of an aging population. To highlight the aging population Table 2.6 shows the percentage of the population less than 10 and 65 and greater. The majority of this change has taken place from 1970-1990.

Table 2.6 Changes in Population Age Distribution, 1930-1990

The differences in the age distribution between years and sexes can influence the results of some mortality calculations. The reasons for this and a computation method to compensate are discussed in Section 2.3.3.1 on standardization.

2.3.2.3 Uncertainty

The population is a dynamic value that changes throughout the year with people immigrating or emigrating, being born or dying. Some other factors affecting population estimates that can contribute to uncertainty include: additions of the Territories and Newfoundland, changes to the method of population estimation, availability of information and use of non-census years.

The Yukon and the North West Territories were not included in the 5-year tabulations of mortality between 1930 - 1955 but were included in the population estimates. The population of the two Territories was less than 0.2% of the total Canadian population during this time and thus their addition caused minimal change to the population-based mortality rates.

Since Newfoundland only joined Confederation in 1949 it was not included in the 5-year population estimates between 1930-1945 but was also not included in the mortality tabulations. Newfoundland represented approximately 2.5% of the population in 1950 and it was simply incorporated into both the mortality rates and the population, causing minimal change.

In 1993 Statistics Canada changed the way they estimated the annual population. There were three changes: non-permanent residents were included, net census undercoverage was accounted for and the reference date for the annual estimates was changed from June 1 to

Table 2.6 Changes in Population Age Distribution, 1930-1990

Gender	Year	9 years and less	65 years and greater
Male	1930	21.1 %	5.4 %
	1950	21.6 %	7.7 %
	1970	20.0 %	7.1 %
	1990	14.6 %	8.7 %
Female	1930	22.0 %	5.5 %
	1950	21.4 %	7.6 %
	1970	19.1 %	8.6 %
	1990	13.5 %	13.2 %

Data Source: Dominion Bureau of Statistics, 1968 and Statistics Canada, 1970 and 1990

July 1. For 1991 these changes resulted in an estimated population increase of approximately one million people (3.6%). These changes affected males more than females. They were also age dependent with the largest changes in the 20-34 age categories. The largest change was approximately 9% in the 20-24 age category (Bender, 1995).

Statistics Canada revised the population estimates back until 1971 which meant there was no point in making changes for the trend information which began in 1930. However, the changes in the population estimates were larger in recent years than in the 70's and 80's (Bender, 1995). As an example of the change, the population for 1990 in Figure 2.2 would be 27.8 million instead of 26.6 million. The 1993 information is based on the revised population estimates which means there will be a difference of a few percent between the 1990 and 1993 mortality rates. While a change of a few percent may seem small, it is a useful reminder that the population is only an estimate which can be altered because of a change in policy regarding which persons should be included.

Available population estimates between 1930-1975 did not include separate age categories for 0-1 and 1-4. To promote comparisons with later years it was assumed the listed 0-5 population estimate had a uniform distribution and was multiplied by 0.2 for the 0-1 age category and 0.8 for the 1-4 age category. Making this calculation for 1993 information resulted in an overestimate for the male population of 2.7% and for the female population of 3.5% in the 0-1 age category. The difference in estimated population was less than 1% in the 1-4 age categories.

The 1980 population was used instead of the 1981 population for trend evidence. This was due to the confusion of not having the mortality information available for 1980 and relying instead on the 1981 information. The difference in population estimates between 1980 and 1981 was approximately 1.2%.

The census took place one year following the five-year increments used. However, because of the delay of approximately two years in publishing the vital statistics, the populations for the selected five-year intervals were only extrapolated back one year, not ahead four years. The difference in values is likely less than the those from other uncertainties in population estimates.

Considering all these factors together the total population estimates have an uncertainty of a few percent (less than 5%). Individual age categories usually have an uncertainty of less than 10%.

2.3.3 Population Based-Rates

Population-based rates are used to compare mortality between different exposed populations. These rates are a ratio of the number of people affected in one group (i.e. dying) versus the total number of people in that same group. This ratio is then multiplied by a standard base (e.g. 1,000 or 100,000) selected for that type of rate and expressed as the number of deaths per base number.

Tables 2.7 to 2.10 are examples showing how population-based rates are being used. A base number of 1,000 is used in the Tables 2.7 and 2.10 while base number of 100,000 in the Tables 2.8 and 2.9. Larger bases are used when rates are smaller to keep the rate numbers from being small fractions. Tables 2.7 to 2.9 are rates expressed as deaths per population while Table 2.10 is expressed as deaths per live births.

Table 2.7 Crude Death Rate Example, 1930 and 1990
Table 2.8 Cause Specific Death Rate Example, 1993
Table 2.9 Age-Specific Death Rate Example, 1993
Table 2.10 Infant Mortality Rate Example, 1930 and 1990

Other examples of mortality rates:

- maternal death rate (annual deaths of mother resulting from pregnancy / annual live births) * (10,000)
- marital status death rate (annual deaths in specific marital status category / total population in marital status category) * (100,000)
- provincial death rate (annual deaths in specific province / total population of province) * (1,000)

Population-based rates can also incorporate participation relating to factors like occupational risks or transportation risks. However, the idea of using a base of those participating in any given risk is discussed in Section 3 on indirect evidence because this is based on a person's behaviour (risk factor).

Table 2.7 Crude Death Rate Example, 1930 and 1990

Year	Gender	Deaths	Population	Crude Annual Death Rate (deaths per 1,000 population)
1930	Male	59,109	5,271,700	11.2
	Female	50,197	4,936,300	10.2
	Both	109,306	10,208,000	10.7
1990	Male	103,968	13,104,200	7.9
	Female	88,005	13,479,800	6.5
	Both	191,973	26,610,400	7.2

Crude Death Rate (annual number of deaths in specified sex group/ total population in specified sex group) * (1,000)

Note: these are crude death rates since differences in age distribution between years and sexes are not included in the calculation. The standardized rates are shown in section 2.3.3.1

Table 2.8 Cause Specific Death Rate Example, 1993

Year	Cause	Deaths	Population	Cause Specific Death Rate (deaths per 10,000 population)
Male	Infectious	1,596	14,343,108	1.1
	Cancer	28,866	14,343,108	20.1
Female	Infectious	659	14,597,489	0.5
	Cancer	23,560	14,597,489	16.1

Cause Specific Death Rate (annual number of deaths from specific cause in specified sex group/ total population in specified sex group) * (10,000)

Note: these are crude death rates since differences in age distribution between sexes are not included in the calculation.

Table 2.9 Age-Specific Death Rate Example, 1993

Age Categories	Deaths	Population	Age Specific Death Rate (deaths per 100,000 population)
Less than 1	2,448	388,394	630
10-14	366	1,962,907	19
40-44	3,846	2,203,697	175
80-84	30,934	417,541	7,409

Age Specific Death Rate (annual number of deaths in specific age group / total population in specified age group) * (10,000)

Table 2.10 Infant Mortality Rate Example, 1930 and 1990

Year	Deaths	Live Births	Infant Mortality Rate (deaths per 1,000 live births)
1930	22,677	~ 250,000	90.6
1990	2,766	~ 407,000	6.8

Infant Mortality Rate (annual deaths less than one year of age / annual live births) * (1,000)

Data Source: see Tables 2.3 and 2.4

2.3.3.1 Age-Standardization

Age-standardization is used to compare two or more populations with different age distributions. Figure 2.3 highlights two groups where differences in age distribution exist: between sexes and between years. Provinces and other geographic areas also have differences in age distribution. Without standardization, the only way to accurately compare mortality rates is to include the breakdown into individual age categories. Many of the figures in this section do include breakdown into age categories and therefore do not require age-standardization.

However, it is often not feasible to include all the age categories, especially in a table or when comparing several years at once. For this reason a process called age-standardization is done using the following equation:

$$\textbf{age-standardized death rate} = \frac{\sum_{i=1}^{n}\left(\frac{d_i}{p_i}\right)P_i}{\sum_{i=1}^{n}P_i}$$

i = age category (1, 2, 3, ... n)

n = 20 (for 1993 evidence), 19 (for trend evidence 1930 to 1990)

d_i = for age category i, the age and/or sex specific number of deaths for a specific cause and/or location

p_i = for age category i, the age and/or sex specific population for a specific cause and/or location

P_i = for age category i, the age specific population (1991 standard population, both sexes combined)

(d_i/p_i) represents the death rate for an individual age category (e.g. annual number of deaths in 5-9 age category divided by the population in the 5-9 age category for a specified year). This rate is then standardized to P_i the standard population. The standard population is the population distribution (for both sexes combined) that other comparison distributions will be adjusted to. The same standard population is used in all age-standardized rate calculations so results are comparable. Presently the 1991 final postcensal population is being used as the standard population. The number of people in the standard population has no effect on the result, it is the distribution of this population by age that alters the final result. Table 2.11 presents age-standardized death rates for 1930 and 1990.

Table 2.11 Crude and Age-Standardized Death Rates, 1930 and 1990

Table 2.11 Crude and Age-Standardized Death Rates, 1930 and 1990

Year	Gender	Crude Death Rate (deaths per 1,000 population)	Age-Standardized Death Rate (deaths per 1,000 population)
1930	Male	11.2	16.5
	Female	10.2	15.1
	Both	10.7	15.8
1990	Male	7.9	9.4
	Female	6.5	5.5
	Both	7.2	7.2

Data Source: see Table 2.4

Notice that in the last row, the crude and standardized death rates are the same. This occurs because the age distribution of both genders combined in 1990 is very similar to the age distribution of the standard population from 1991. However, in 1930, the standardized rate for both is almost half as great as the crude rate. This is caused by the large difference in the age distributions between 1930 and the standard population from 1991. In 1930 the population was on average younger than in 1991 (see Figure 2.3). The age-standardized rate calculates that if 1930 had the same population age distribution as 1991 (i.e. older) and the same total number of people died at the 1930 rates for each age category, the effect would be 50% more total deaths.

An adjustment also occurs between males and females. In 1990, the age-standardized rate for males increased (7.9 to 9.4) while for females it decreased (6.5 to 5.5). Similar to 1930 being younger on average than the 1991 standard population, the 1990 male population is younger on average than the female population which increases the male age-standardized rate. Since females are older on average than males, the female age-standardized rate decreases.

Calculating age-standardized rates is called direct standardization and is the only standardization method used for direct evidence. If age specific death rates for subgroups are not available then a method called indirect standardization can be used. Indirect standardization calculates a ratio, usually called the standardized mortality ratio (SMR) but it is not reviewed here because information was available for direct standardization.

2.4 Total Registered Death Evidence

The annual number of deaths is the starting value from which all other annual mortality evidence derives. Divisions are made based on sex, age, marital status, residence and cause of death with varying degrees of increased uncertainty. Deaths of non-Canadian residents are not included in these totals. Deaths of Canadians which occur in the United States are included in the Canadian totals under a mutual agreement. Otherwise, it is assumed that deaths of Canadians in foreign countries are normally not included.

2.4.1 1993 Evidence

In 1993 a total of 204,912 death were registered. This corresponds to a crude death rate of 7.1 deaths per 1,000 population. Corresponding measures of the number of death are:

- 1 in 141 annual chance of dying over the entire population
- 561 deaths per day
- 23 deaths per hour
- 1 death every 2.5 minutes

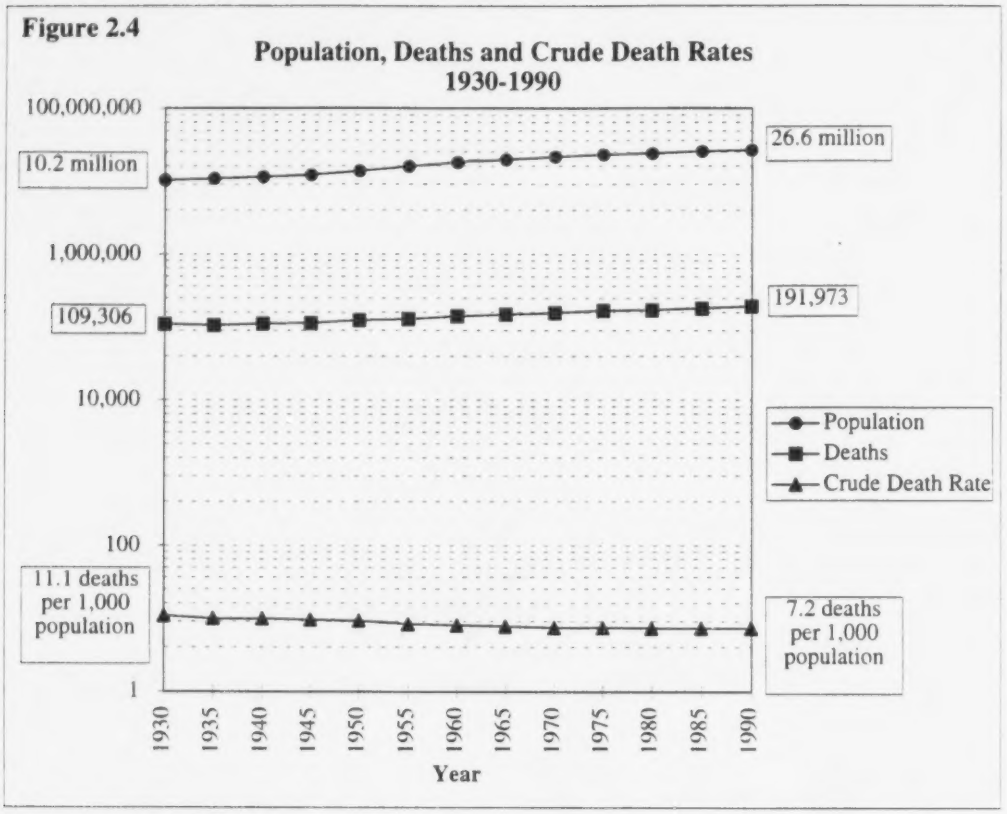
2.4.2 Trend Evidence

The Yukon and North West Territories were not included in the annual totals for the information collected between 1930-1955 because they were not regarded as complete and have little difference on the totals for the rest of Canada. For the years collected, the combined deaths of the two Territories was less than 0.5% of the total number of deaths in the rest of Canada.

Figure 2.4 Population, Deaths and Crude Death Rates, 1930-1990

Figure 2.4 shows the population, deaths and crude death rate from 1930 to 1990. These three elements were combined on one figure to show the relationship between population, deaths and the crude death rate. The crude death rate was shown earlier in Section 2.3.3. For this figure only, it is important to recognize that the y-axis has two different meanings. For population and deaths it is an annual number but for crude death rate it is the annual deaths per 1,000 population.

Figure 2.4



Data Source: see Table 2.4

Between 1930 and 1990 the population increased 2.6 times while the number of deaths increased 1.7 times. The greater increase in the population in comparison with total deaths explains why the crude death rate has been decreasing.

2.4.3 Uncertainty

The total annual number of deaths is the most accurate piece of mortality evidence available. Of those people registered, there is little doubt about whether or not they have died. However, there is uncertainty associated with whether all the deaths are known and whether they have all been included in time for the annual publication of mortality statistics.

Knowing how many deaths are unknown and not registered is impossible. More deaths were likely not registered earlier in this century than now, especially in the more remote areas of Canada.

Statistics Canada publishes their annual reports relating to vital statistics within time constraints. In 1990 there were 84 late registrations which were not included in the reports. However, this discrepancy was less than 0.05 % of the registered total deaths of 191,973 (Statistics Canada, 1995b).

2.5 Evidence of Sex Differences

Wilkins in the opening paragraph of a paper called 'Causes of death: How the sexes differ' writes:

> "Biological, social and behavioural factors have resulted in differences in the most common causes of death for males and females. In infancy, the causes are similar, but start to diverge sharply. However, as people advance into their senior years, differences in the leading causes of death for men and women tend to diminish." (Wilkins, 1995, pg. 33)

This quote highlights some general factors that are associated with differences in mortality between sexes which will be discussed in more detail in the Section 3 on indirect evidence. Because the differences are relatively large and consistent, where possible all numbers will be presented separately for males and females.

2.5.1 1993 Evidence

In 1993 there were 109,407 registered male deaths and 95,505 registered female deaths. The crude deaths rates, in deaths per 1,000 population, were 7.6 for males and 6.5 for females. The larger number of male deaths (13% larger) and the smaller number of males in the population (2% smaller) meant the crude death rate for males is 14% larger.

2.5.2 Trend Evidence

Deaths separated by sex are summarized for the years 1930-1990.

Figure 2.5 Total Deaths by Sex, 1930-1990

Figure 2.5 shows the deaths for males and females between 1930 and 1990. There have consistently been a greater number of deaths in males than females. This difference increased steadily from 1930, peaked in the 1960's and has since been decreasing. In 1960 and 1965 there were 29% more deaths in males and females but by 1990 this had decreased to 15%.

Figure 2.6 Crude Death Rate by Sex, 1930-1990

Figure 2.6 shows the crude death rate for males and females between 1930 and 1990. Since the population has been increasing more rapidly than deaths, there has been a general

Figure 2.5

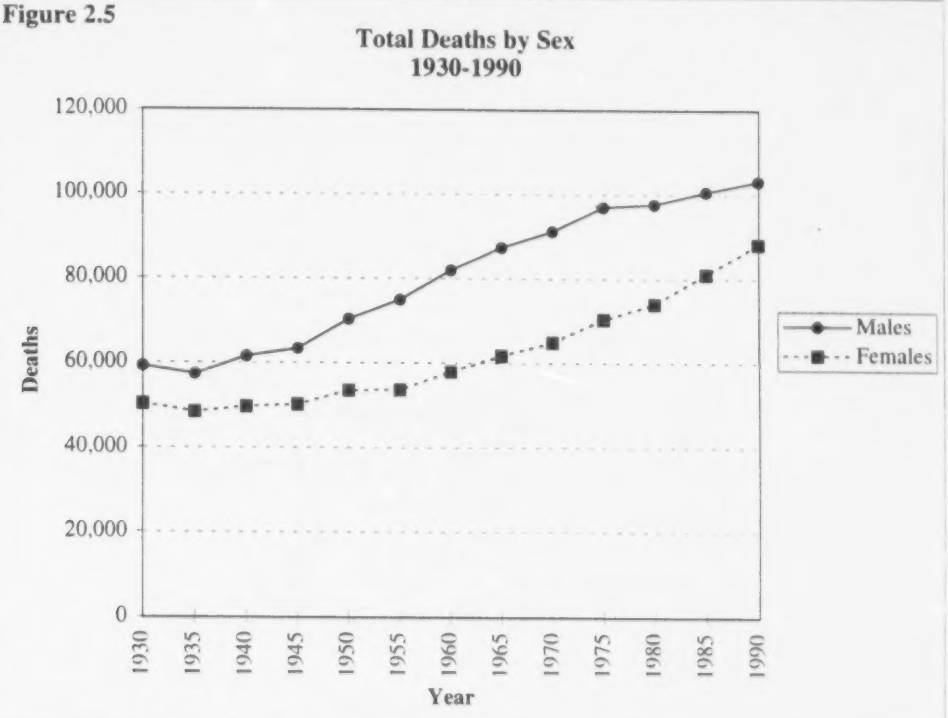
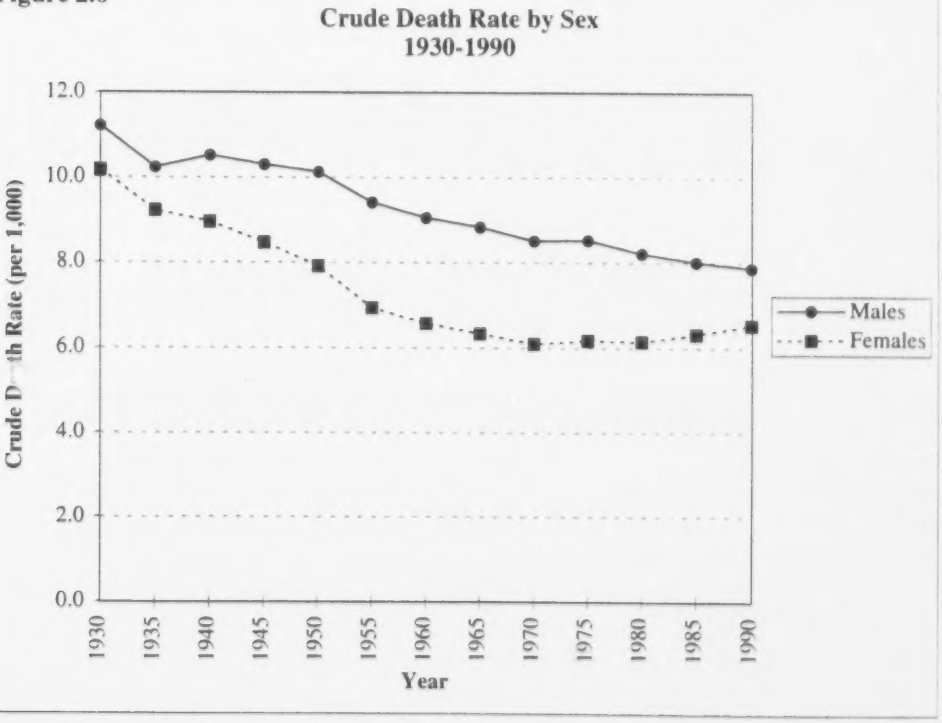


Figure 2.6



Data Source: see Table 2.4

lowering in the crude death rate. Caution needs to be used with this figure since the crude rates are not age-standardized. Figure 2.11 compares the crude and age-standardized rates, highlighting the importance of compensating for changing population age distributions.

2.5.3 Uncertainty

None of the cause of death summaries reported that the sex was not known or was uncertain. It is likely that any errors in recording the sex are very small. Overall, the uncertainty in number of deaths by sex will be slightly greater than (or at a minimum equal to) the uncertainty in the number of total registered deaths (see Section 2.4.3). Overall this is likely less than 0.1%.

2.6 Evidence on Age

Age and mortality are strongly related. This section summarizes the relationship between age and mortality including separate subsections on infant deaths (less than one year of age) and life expectancy.

In most cases two figures are included to summarize a set of information. The first figure shows the number of deaths and the second the death rate. The total number of deaths must be interpreted carefully for two reasons. The first is that all the age categories are not the same number of years. The first category is for only less than 1 year, the second is for four years (1-4), then every category is five years until the last category which includes all people above a certain age (for 1993 information 90+, for 1930-1990 information 85+). The second reason to interpret the total number of deaths figure is large differences in population between different age categories and between sexes. As shown earlier in Table 2.5, differences in the population of age categories with the same five year span can be 10 to 20 fold. This is why the second figure is included. By dividing by the population the differences in population between age categories is accounted for.

2.6.1 1993 Evidence

Deaths separated by age and sex are summarized for 1993.

Figure 2.7 Total Deaths by Age, 1993

Figure 2.7 shows the total number of deaths for different age categories in 1993. This figure can be used to identify how many males and females died in any age category. For example in 1993 just over 2,000 females died at an age of between 50 - 54. Care must be taken in attempting conclusions from this figure because it does not take into account the differences in population between age categories. While there is a sharp drop in the number of male deaths past 85 years of age, there is an even sharper drop in the number of males alive. This is why Figure 2.8 showing the death rate is included.

Figure 2.8 Death Rate by Age, 1993

Figure 2.8 shows the death rate for different age categories in 1993. Several conclusions can be drawn from this figure. Males are more likely to die than females in all age categories. The chances of dying in the first year of life are similar to the chances of

Figure 2.7

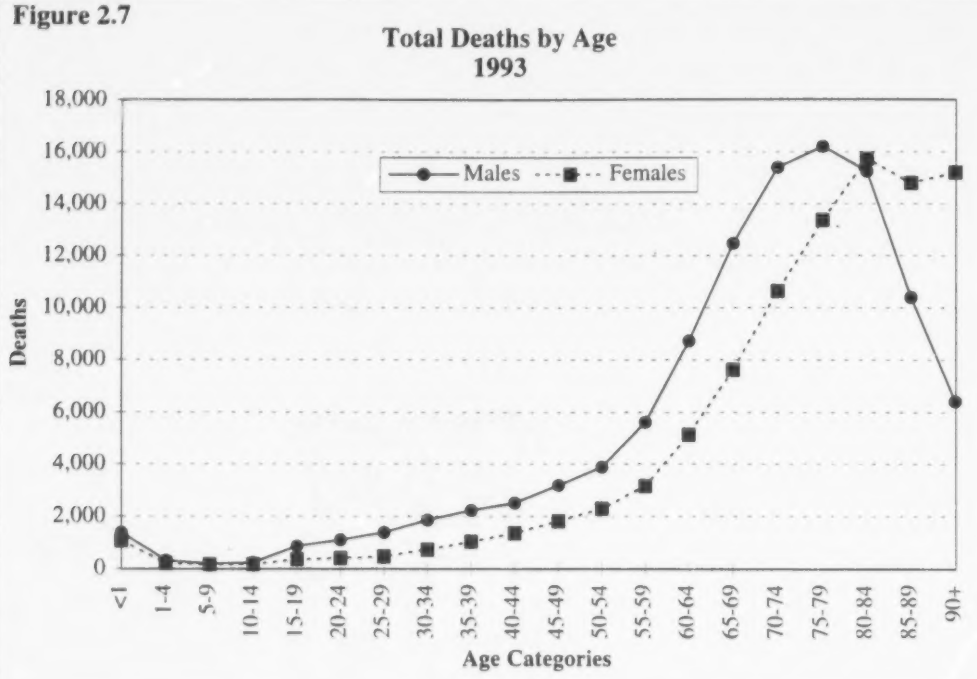
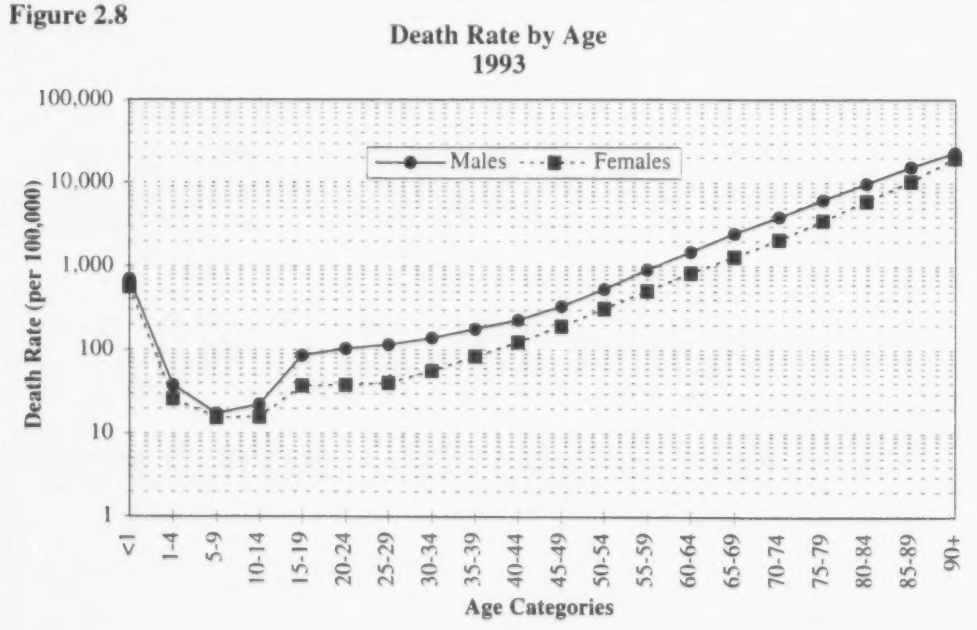


Figure 2.8



Data Source: Statistics Canada, 1995a

someone dying in their mid to late fifties. After the first year of life, the risk of dying drops dramatically (approximately 20 times lower) until past middle age.

2.6.2 Trend Evidence

Deaths separated by age and sex are summarized for the years 1930-1990.

Figure 2.9 Total Deaths by Age, 1930-1990

Figure 2.9 is similar to Figure 2.7 except the sexes are combined and four different years are compared. Care must be taken interpreting this figure because it does not take into account the differences in population between age categories and years (the population increased 2.6 times between 1930 and 1990). In both 1930 and 1950, more people died in the first year of life than in any other age category.

Figure 2.10 Death Rate by Age, 1930-1990

Figure 2.10 is similar to Figure 2.8 except instead of only one year, four different years are compared. The overall pattern of a high initial death rate followed by a rapid decrease and then a exponential increase with age is similar over the 60 years between 1930 and 1990. However, there is a significantly lower death rate in all age categories today than in 1930. The largest reduction in the death rate over this 60 year period has occurred in the first 15 years of life. Between 1930 and 1990 the chance of dying in the first year of life has decreased by a factor 14. There is additional information on infant deaths in Section 2.6.3.

Figure 2.11 Crude and Age-Standardized Death Rates, 1930-1990

Figure 2.11 shows the crude and standardized death rates for males and females between 1930 and 1990. Crude rates have shown a lowering trend since 1930 with a slight increase for females between 1980 and 1990. However, standardized rates show a larger and consistent decrease for both males and females. The difference between the two rates is entirely due to differences in the population age distribution between sexes.

This figure shows why using crude rates can be misleading. Without considering the aging population since 1930, the reduction in death rates appear much lower. The standardized rates not only highlight the larger decrease in death rates from 1930 to 1990 but also the difference between males and females which is actually greater than indicated by the crude rates.

Figure 2.9

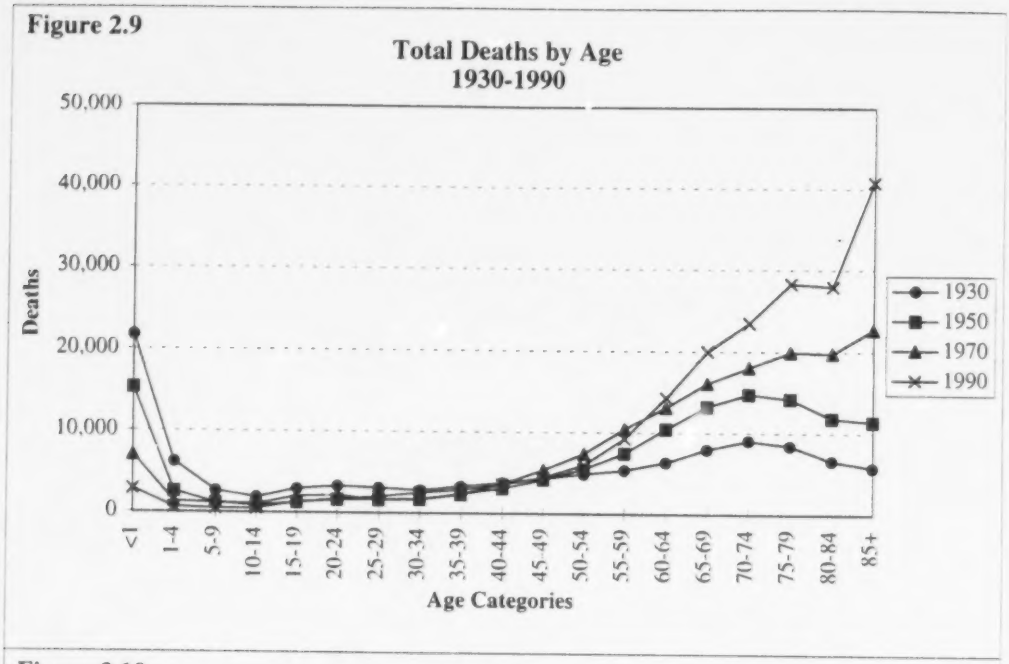
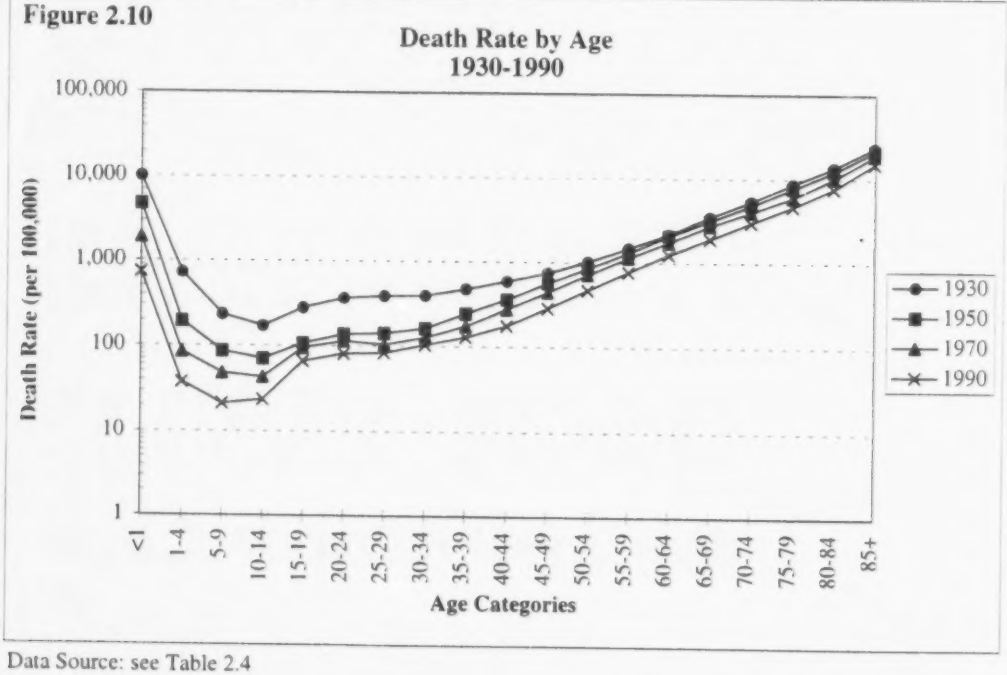
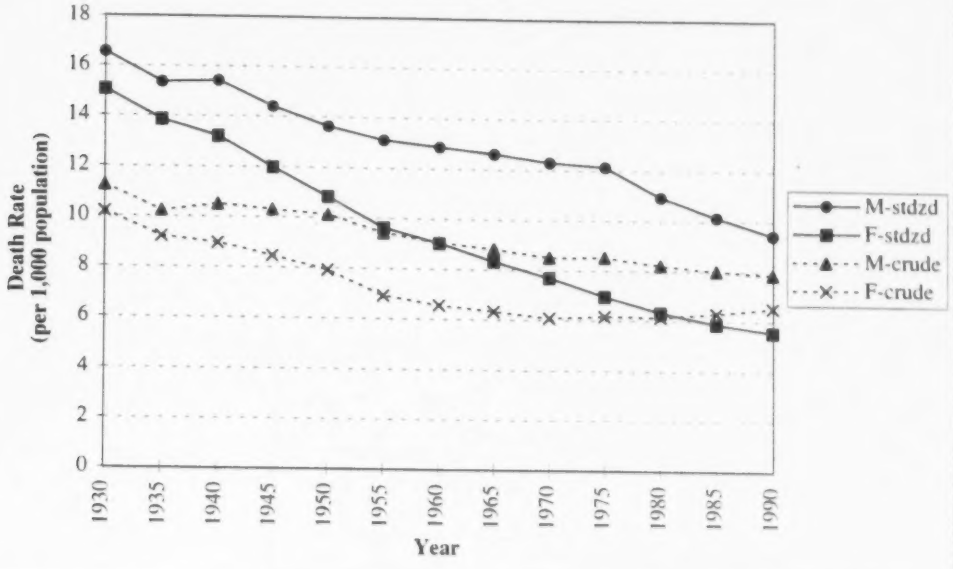


Figure 2.10



Data Source: see Table 2.4

Figure 2.11 **Crude and Age-Standardized Death Rates 1930-1990**



Data Source: see Table 2.4

2.6.3 Infant Deaths

Infant deaths refer to those occurring at less than 1 year of age. Infant death rates, in addition to life expectancy, are often used as a measure of the prevailing health in a country and is a reflection of several factors including the medical system. In addition to measuring the care of the newborn, the infant death rate also reflects the health of the community and may be assumed to reflect the health of parents (Alderson, 1988).

If information is available it is possible to standardize infant mortality rates using birth weight. This additional evidence was beyond the scope of this thesis but a more in depth analysis of infant deaths should include birth weight information.

2.6.3.1 1993 Evidence

In 1993 there were a total of 2,448 infant deaths (1,379 males and 1,069 females). There were a total of 388,394 live births in 1993 and the corresponding infant mortality rate was 6.3 per 1,000 lives births.

2.6.3.2 Trend Evidence

Infant deaths separated by sex are summarized for the years 1930-1990.

Figure 2.12 Total Infant Deaths, 1930-1990

Figure 2.12 shows the number of infant deaths between 1930 and 1990 for males, females and both combined. Care must be taken in drawing conclusions from this figure because it does not account for the number of births that actually took place each year. The total number of infant deaths decreased by a factor of 8 from 22,677 in 1930 to 2,766 in 1990.

Unlike most other figures, where using five year intervals was adequate because of relatively consistent annual changes over time, the number of infant deaths from year to year fluctuated more significantly. Not shown in the figure is information for 1936-1938 where the infant deaths were 15,442, 17,762 and 15,233. This increase in 1937 was not due to increased births.

Figure 2.13 Infant Mortality Rate, 1930-1990

Figure 2.13 shows the infant death rate between 1930 and 1990 for males, females and both combined. The infant death rate decreased by 13 times from 90.6 per 1,000 live births in 1930 to 6.8 per 1,000 live births in 1990.

Figure 2.12

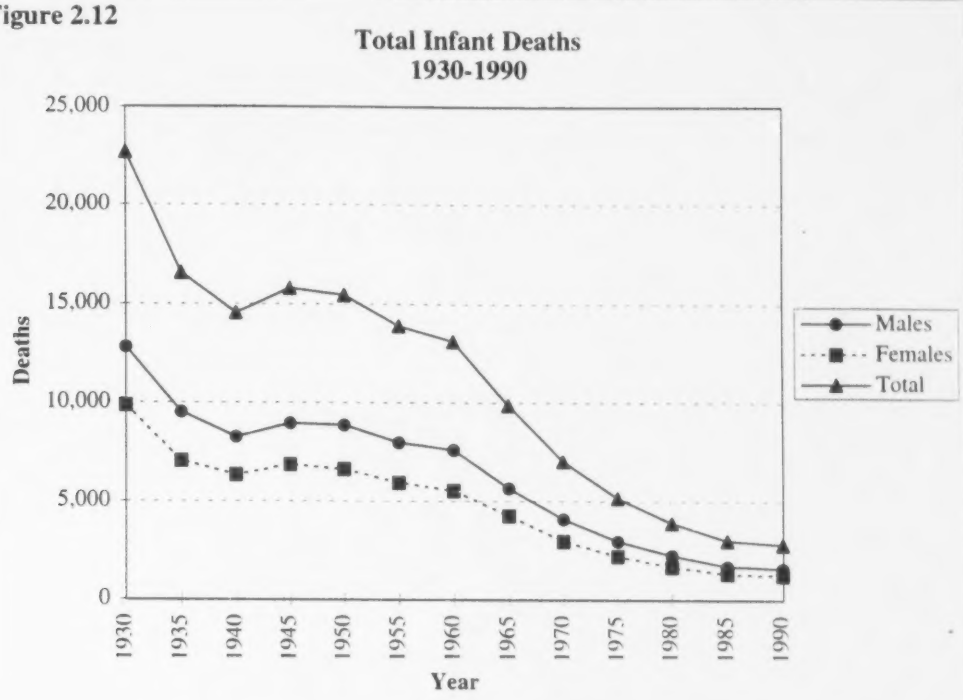


Figure 2.13

Data Source: Statistics Canada, 1994c

2.6.4 Life Expectancy

Life expectancy is commonly used as a measure of a countries health. Canada currently enjoys one of the highest life expectancies in the world. Life expectancy can also summarize trends in health over time. Canada's life expectancy has changed significantly over the past century.

Life expectancy is the median age of death of people dying in a given year. For example, if 100,000 males died in a particular year, they would be ranked by the age at which they died. The age of the 50,000th male (the median male) would represent the life expectancy for that particular year. The correct method for calculating life expectancy is by using a life table.

The term life expectancy is misleading because so far people born earlier in this century have lived much longer than the life expectancy based on the year they were born. Life expectancy is a dynamic quantity which has historically increased by several months a year. However this trend is currently less significant because annual increases in life expectancy have been lower. Only when life expectancy becomes relatively constant over a period of observation will it be accurate for predicting future rates.

2.6.4.1 1993 Evidence

In 1993 the life expectancy for Canadians was 78.0 (74.9 males and 81.0 females) (Statistics Canada, 1996).

2.6.4.2 Trend Evidence

Life expectancy according to age and sex are summarized for the years 1930-1990.

Figure 2.14 Cumulative Percentage of Deaths by Age

Figure 2.14 shows the cumulative percentage of deaths by age for 1930, 1950, 1970 and 1990. This figure could have been presented earlier but it serves as a good introduction to life expectancy. The point at which the line for each year crosses the 50% (or median) determines the life expectancy for that year. The life expectancy has increased substantially between 1930 and 1950 and steadily at a lower rate over each of the next 20 years. Figure 2.14 highlights where most of the gains in life expectancy have arisen. In 1930, 20% of

Figure 2.14

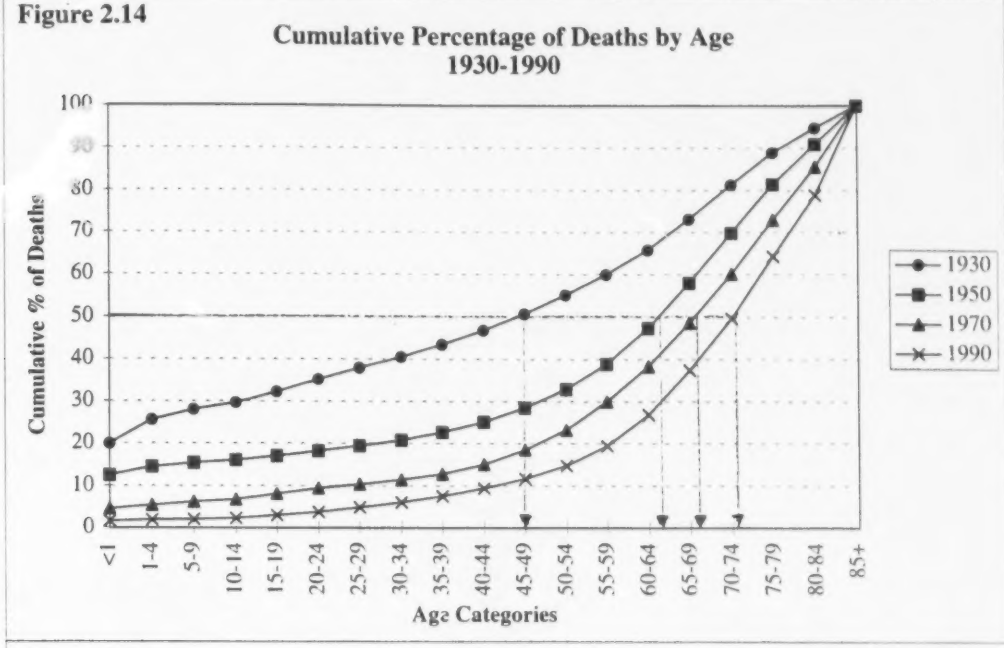
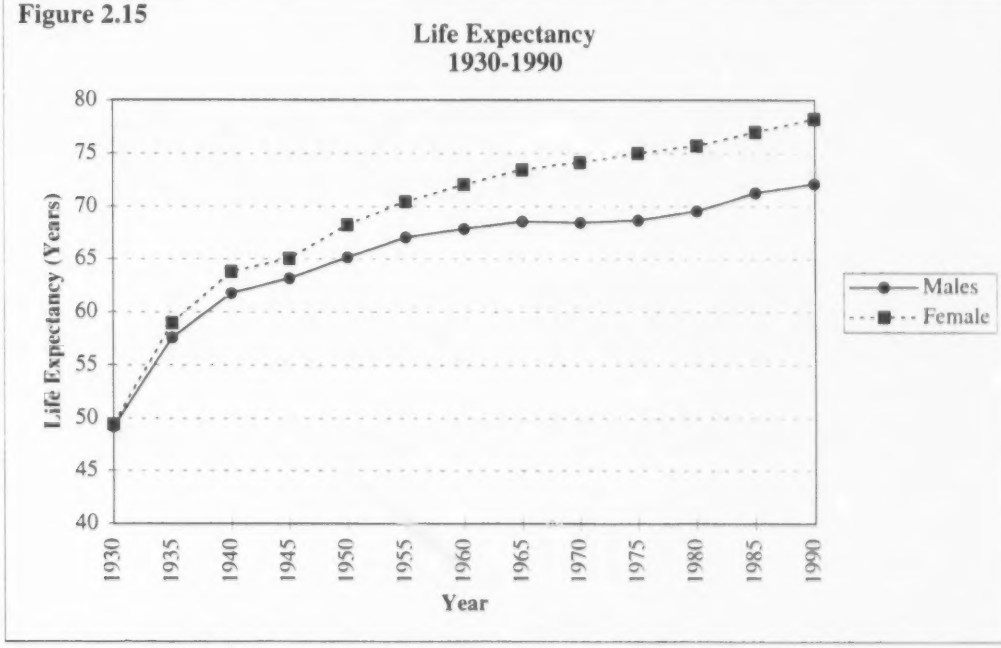


Figure 2.15



Data Source: see Table 2.4

people did not survive past one year of age and the mortality increased more rapidly than the other years. Between 1950 and 1970 it appears most of the increased life expectancy was experienced from a reduction in infant mortality. Between 1970 and 1990 a continuing reduction in infant mortality helped but it appears that starting around the age of forty there was also a reduction in mortality (indicated by the increasing separation of the lines).

Figure 2.15 Life Expectancy, 1930-1990

Figure 2.15 shows the life expectancy for males and females between 1930 and 1990. As shown in the previous figure, a large gain in life expectancy took place between 1930 and 1950 followed by more gradual increases. The life expectancy for females increased at a greater rate than males. In 1930 they were similar but by 1990 there is a 6 year difference in life expectancy.

Figure 2.16 Remaining Life Expectancy at Selected Ages, Males, 1930-1990

Figure 2.17 Remaining Life Expectancy at Selected Ages, Females, 1930-1990

Figure 2.16 and 2.17 show the remaining life expectancy at selected ages between 1930 and 1990 for males and females respectively. The actual years used for this figure are averages of three years centered around the census years. The top line, at birth, is the life expectancy shown earlier. The other lines represent the expected years of life remaining for an individual of the lines age in the different years.

For example, the median number of years of life remaining for a 25 year old male in 1930-32 is 45 and in 1990-92 is 51. Therefore, a hypothetical 25 year old male in 1930-32 could expect to live until 70 (25+45) while a hypothetical 25 year old male in 1990-92 could expect to live until 76 (25+51).

These figures demonstrates that the gain in life expectancy over time has been primarily because of reduced mortality in the younger age groups. Though relatively fewer people reached 80, in 1930, both males and females could expect 6 more years of life while in 1990 a similar aged male could expect 7 more years and a female 10 more years of life.

2.6.5 Uncertainty

The annual publications relating to mortality list the number of deaths where the age was unknown. The number of unknown ages ranged from 85 in 1930 to 3 in 1993. Similar to the total number of deaths and the sex, the age at death is an accurate statistic, with an

Figure 2.16

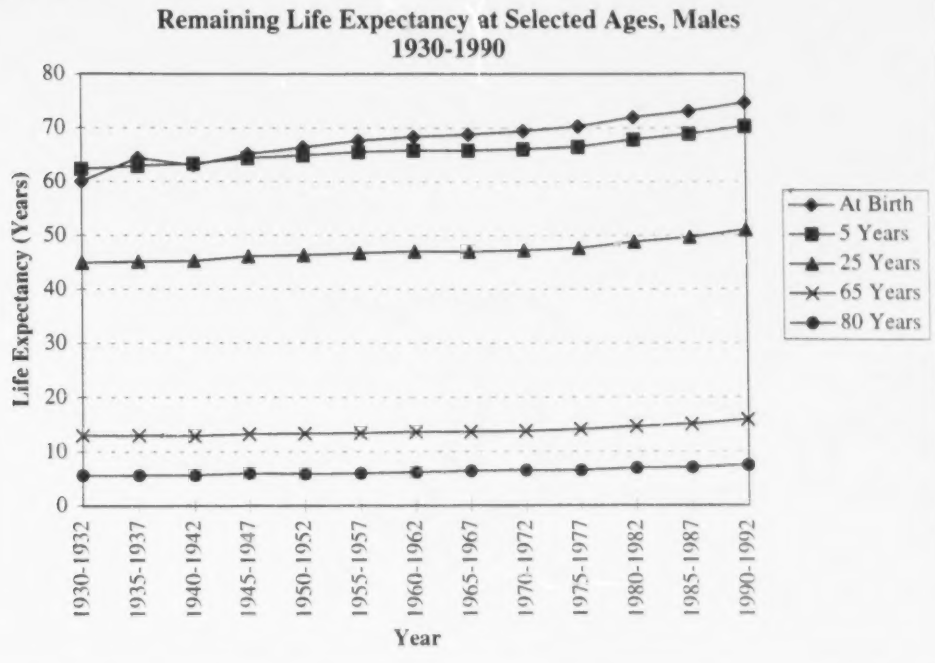
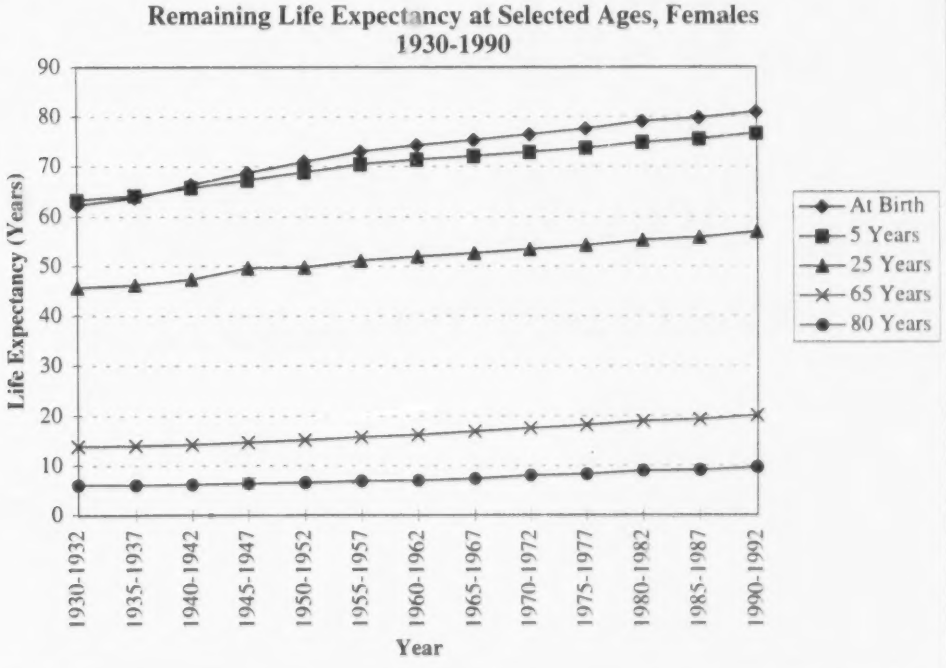


Figure 2.17



Data Source: Statistics Canada, 1994c

uncertainty only slightly greater that the total number of deaths. Over the entire number of reported deaths, uncertainty in age at death is likely less than 0.1%.

2.7 Marital Status Evidence

The measurement of marital status evidence is direct, however reasons for the differences are discussed in Section 3.3.3.5.

Figure 2.18 Death Rate by Marital Status, Males, 1990

Figure 2.18 shows the death rate for different age groups by marital status for males in 1990. The figure shows that the death rate for all three categories of marital status increases with age, as highlighted in Section 2.6. The figure shows that married people had a consistently lower death rate than single and widowed or divorced people. For the first three age categories the death rates were approximately three times lower for married people. For those aged 65+, the difference was approximately two times lower. Because these age categories are fairly large these were not age-standardized some of the differences may be over or under-estimated. For example, it is logical to assume that a married person dying is younger than a widowed or divorced person, so differences in age within each age category may account for some of the apparent difference.

Figure 2.19 Death Rate by Marital Status, Females, 1990

Figure 2.19 shows the death rate for different age groups by marital status for females in 1990. The figure shows that the death rate for all three categories of marital status increases with age, as shown in Section 2.6. Figure 2.19 shows that, similar to married males, married females have a consistently lower death rate than single or widowed or divorced people. For the first three age categories the death rates were two to four times lower for married people, clearly an interesting observation.

Statistics Canada has recently announced they no longer intend to collect information on marital status. This data suggest that would be an enormous error.

2.7.1 Uncertainty

There was no information included concerning the completeness of the martial status information. It is likely that incompleteness is a more important factor than errors in completing the form. However with no additional information, it is assumed that the uncertainty is greater than total registered deaths, sex and age but less, possibly several times than 1%.

Figure 2.18 **Death Rate by Marital Status, Males 1990**

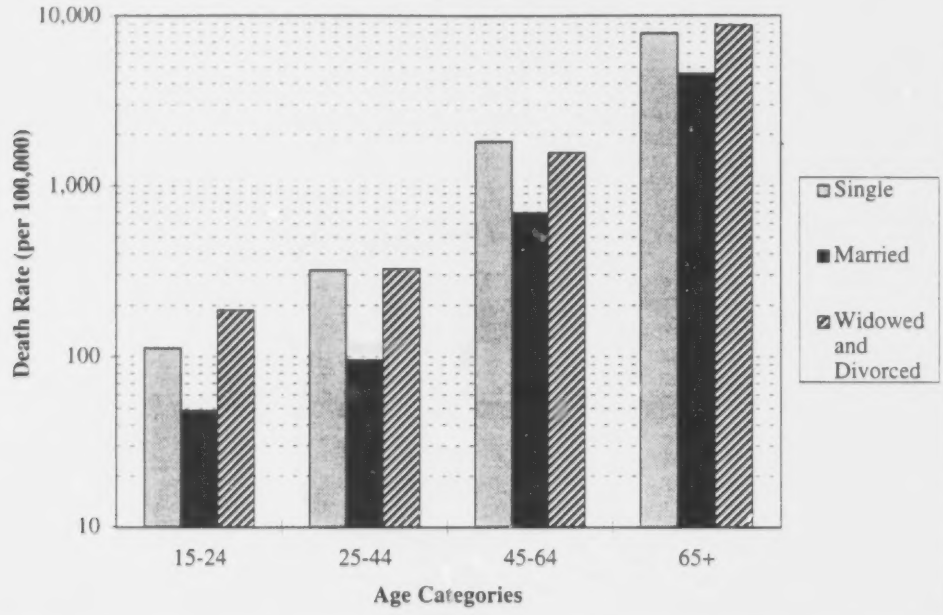
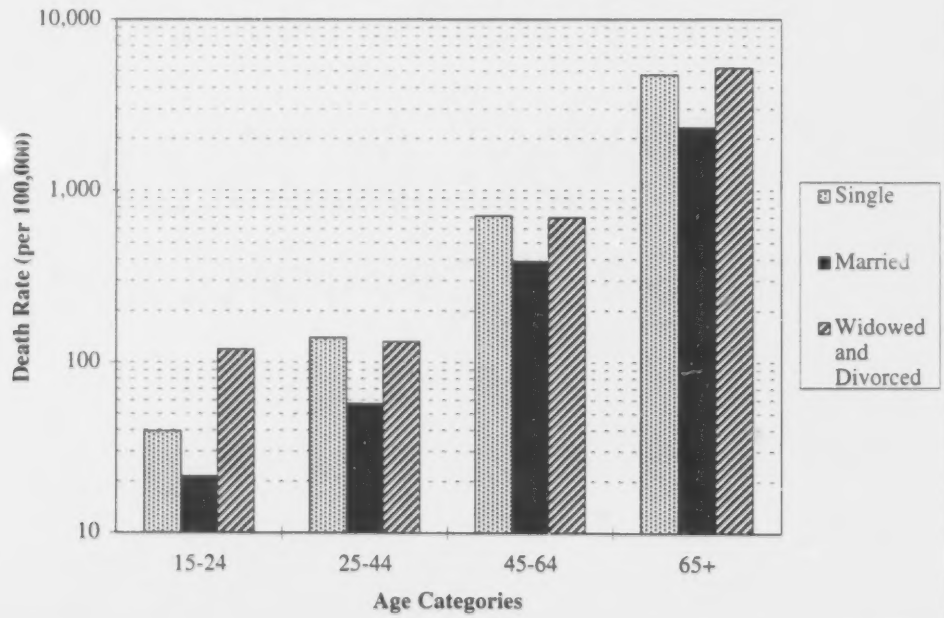


Figure 2.19 **Death Rate by Marital Status, Females 1990**



Data Source: Statistics Canada, 1994c

2.8 Information on Usual Residence

Place of residence is commonly used to compare mortality rates between provinces and territories. On the death registration form, both the place of death and the usual residence are recorded (see Figure 2.1). Divisions can also be made by urban or rural residence, or for more detailed comparisons by counties. Often epidemiological studies will use place of residence and the cause of death to identify locations of disease clusters. More detailed studies are then performed to ascertain any possible associations with risk factors.

For the cause of death in Canada, only mortality rates separated by province are published.

Figure 2.20 Deaths by Province, 1993

Figure 2.20 shows the number of deaths by province for 1993. A significant proportion of all deaths take place in Ontario and Quebec.

Figure 2.21 Age-Standardized Death Rate by Province, 1993

Figure 2.21 shows the age-standardized death rates by province for 1993. The figure shows the large difference in death rates between males and females which is not shown as significant in the previous figure. The age-standardization process emphasized that the males were dying at a relatively younger age than females even though the total number of deaths were only slightly greater. Age-standardized rates must be used when including the territories because they have a significantly younger population relative to the rest of the provinces. Otherwise, comparisons would be meaningless. The crude death rates for the territories are actually lower than those of the provinces.

2.8.1 Uncertainty

No information was included concerning uncertainties in reporting evidence of mortality by province. Because each province collects information within in its own boundaries before sending it to Ottawa for compilation, the provincial assignment should be accurate. The uncertainty is likely only slightly greater than total registered deaths, age or sex.

Uncertainty related to using more detail residential information would be significantly greater.

Figure 2.20

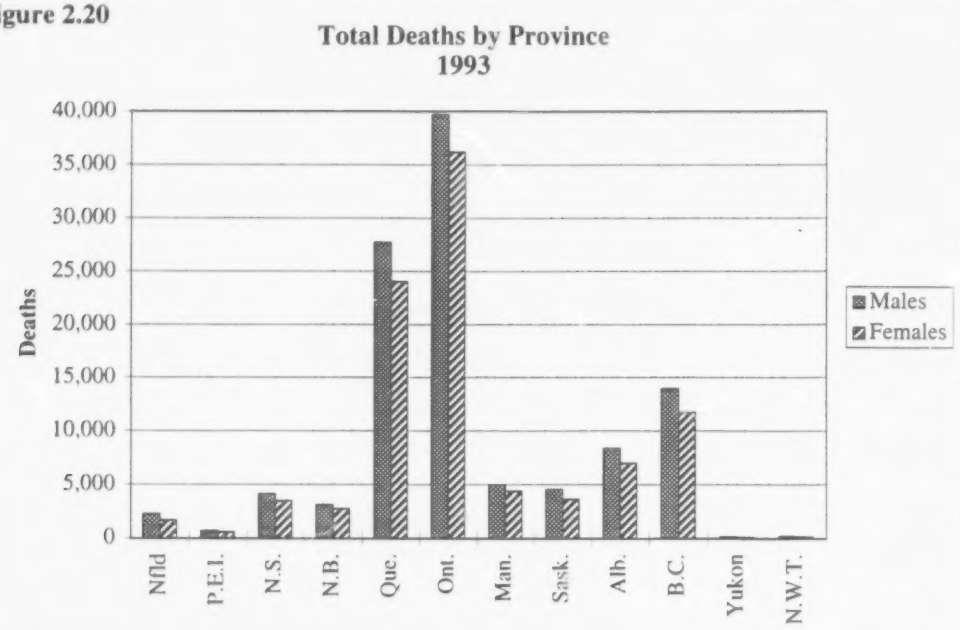
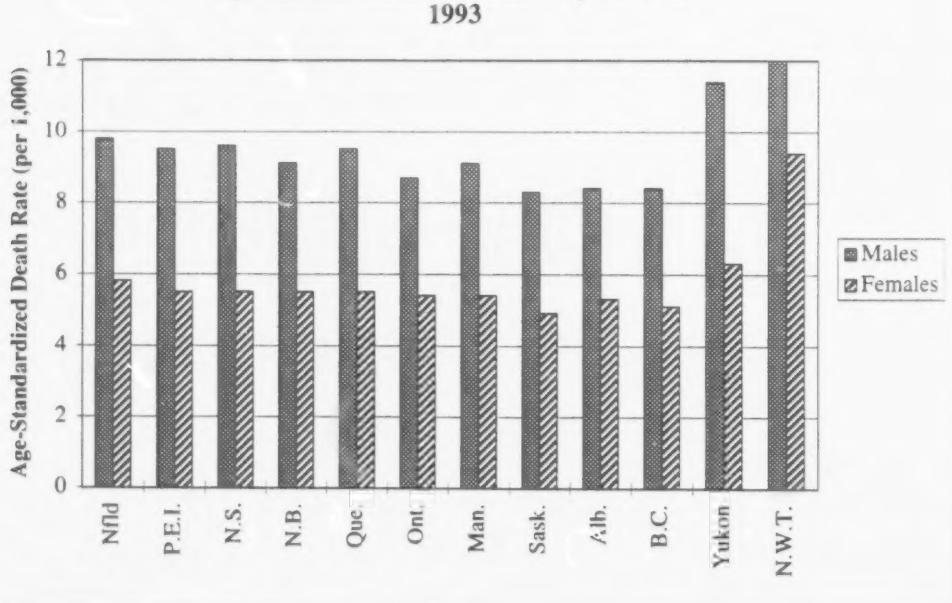


Figure 2.21



Data Source: Statistics Canada, 1995a and 1996

2.9 Cause of Death Evidence

Unlike the other types of direct evidence which are provided by an informant (relative or acquaintance), the cause of death must be filled in by a medical practitioner or coroner. The cause of death is one of the most valuable additional pieces of evidence and adds greatly to the evidence available on causes of mortality. Because it is so different from the other types of direct evidence, extra attention in this thesis has been devoted to explaining the background behind the reported cause the death.

2.9.1 International Classification of Diseases (ICD)

2.9.1.1 History

Classifying cause of death has been a compromise for both medical and statistical purposes. From a medical standpoint, the cause of death could be classified according to several factors including: biomedical cause (etiology), anatomical site and circumstances of onset. From a statistical perspective, cause of death evidence needs to be used for several purposes including: vital statistics, hospitals records, social surveys and illness surveys.

Systematic classification of diseases, including cause of death, began in the 18th century. Modern day classification can be traced back to William Farr who worked for the General Register Office of England and Wales starting in 1837. At the first International Statistical Congress in 1853, Farr and another person were asked to make a list classifying causes of death which would be applicable to all countries. Farr's list, submitted at the next congress in 1855, became adopted in 1864 and underwent revisions over the next three decades. Farr's classification distinguished between particular diseases and those of a particular organ or anatomical site. Farr's classification in 1855 was arranged into five groups: epidemic diseases, constitutional (general) disease, local diseases arranged by anatomical site, developmental disease and diseases that are the direct result of violence. While never universally accepted at that time, Farr's classification served as the basis for the modern day International List of Causes of Death (Alderson, 1988).

In 1891, the International Statistical Institute, the successor to the International Statistical Congress, requested a committee chaired by Jacques Bertillion to prepare a classification of causes of death. At the meeting in 1893 Bertillion presented his report which was based on the same principles as Farr.

In 1898, the American Public Health Association, which included participants from Canada, adopted the Bertillion Classification. The first International Conference for the review of the Bertillion (or International Classification of Causes of Death) took place in 1900 with delegates from 26 countries. In addition to this first review it was proposed that the classification be reviewed every 10 years. The second conference took place in 1909, the third in 1920, the fourth in 1929 and the fifth in 1938.

A major change took place in 1948 at the sixth conference when the World Health Organization (WHO) took responsibility for organizing the classification scheme. Major changes at this conference included adopting a comprehensive list for mortality and morbidity and agreeing on rules for selecting the underlying cause of death. Subsequent conferences organized by the WHO took place in 1955 (seventh), 1965 (eighth) and 1975 (ninth) (WHO, 1975).

Discussion of the tenth revision began earlier than usual because the changes which are planned are major. Two major changes include using an alphanumeric coding scheme and having it be the core for several health related classifications. For this reason, the usual ten year revision cycle was increased to fourteen, however further delays have occurred. The implementation of the tenth code in Canada is anticipated for 1996 (Taylor, 1992).

2.9.1.2 Underlying Cause of Death

The Medical Certificate of Death is section 21 of the Death Registration Form (Figure 2.1). This section is divided into two parts:

- Part I is for the sequence of events leading to the death and proceeds backwards from the immediate cause
- Part II is for other significant contributions to death

For some cases of death only Part I needs to be filled in, for others all parts must be filled in. The last cause listed in Part I is termed the underlying cause of death (UCD). This term was established at the 6th conference on the ICD. For our purposes it is the most important cause since this is what is used in the published statistics. The underlying cause of death is defined as:

> "(a) the disease or injury which initiated the train of events leading directly to death, or
> (b) the circumstances of the accident or violence which produced the fatal injury." (WHO, 1975, pg. 763)

The following are three examples from WHO booklet (1979) which provide an idea of the types and potential confusion involved in ascertaining the underlying cause of death.

Example 1

A man of 47 without previous history of coronary disease suffered a myocardial infarction and died 24 hours later.

I (a) Myocardial infarction

In this case the UCD is myocardial infarction as well as the immediate cause of death.

Example 2

A woman of 59 died of asphyxia following inhalation of vomitus some hours after suffering a cerebellar haemorrhage. Three years previously she had been diagnosed as having adrenal adenoma with aldosteronism which manifested itself as hypertension. Congestive heart failure was also present.

I (a) Asphyxia by vomitus
(b) Cerebellar haemorrhage
(c) Hypertension
(d) Aldosteronism
(e) Adrenal adenoma
II Congestive heart failure

In this case extra lines were needed and the UCD is a benign neoplasm of the adrenal gland.

Example 3

A man of 49 died of a fracture of the vault of the skull shortly after being involved in a collision between the car he was driving and a heavy truck on a narrow road.

I (a) Fracture of vault of skull
(b) Collision between car he was driving and heavy truck, on road

In this case the UCD is collision between a motor vehicle and another motor vehicle, deceased person specified as driver.

One potential future development relating to the cause of death is the use of multiple cause coding. Instead of only recording the underlying cause of death, all the causes may be recorded in the database (they are always available on the original death certificates). This may provide useful additional information for subsequent studies. Some provinces have already begun to record multiple causes in their databases. The use of multiple cause coding in referred to by Alderson (1988) and Nam (1990).

2.9.1.3 Cause of Death Categories

Since the 6th revision of the ICD in 1960, the same 17 categories (I-XVII) have been used as the first division of causes of death. Table 2.12 lists the seventeen major categories with both their full names and a shortened name. The full name is that used in the ICD and the summaries by Statistics Canada. The shortened names were selected for this thesis to simply tables and discussion.

Table 2.12 Major Categories and Shortened Names of Causes of Death

Each of the 17 categories have being divided into subcategories (ranging from none to 22 subcategories). As an example the first category, Infectious, (ICD-9, 001-139) has 16 subcategories (001-009, 010-018, 020-027 ... 137-139). Each three digit number represent one cause of death and sometimes an additional fourth digit, a decimal, is also added. There are spaces left intentionally in the numbering system so that there are not 1000 distinct 3-digit codes (001-E999). These spaces allow new subcategories to be added if needed such as 042-044 (HIV Infection).

Canada is currently using the four digit ICD code. In most cases however, the fourth digit is not useful because it is not consistently recorded. There are usually a large number of 'unspecified' fourth digits. The following table is an example of the different divisions within the ICD system. The example starts with a four digit code for a malignant neoplasm of the sigmoid colon (a specific section of the colon) and works backwards.

Table 2.13 Example of 4 Digit ICD-9 Coding

2.9.1.4 Summary Lists

The ICD actually contains two level of coding which are both used by Statistics Canada in reporting the mortality data. The first is the annual Causes of Death which contains the detailed four digit codes. This was the main source of information for 1993. The second is a summary list of approximately 280 individual causes of death, with no extra levels of detail. This is published in an annual publication called Mortality - Summary List of Causes.

Table 2.12 Major Categories and Shortened Names of Causes of Death

No.	Code	Family Name	Shortened Name
I	001-139	Infectious and Parasitic Diseases	Infectious Diseases
II	140-239	Neoplasms	Cancer
III	240-279	Endocrine, Nutritional and Metabolic Diseases and Immunity Disorders	Endocrine and Others
IV	280-289	Diseases of Blood and Blood-Forming Organs	Blood Diseases
V	290-319	Mental Disorders	Mental Disorders
VI	320-389	Diseases of the Nervous System and Sense Organs	Nervous System Diseases
VII	390-459	Diseases of the Circulatory System	Cardiovascular Diseases
VIII	460-519	Diseases of the Respiratory System	Respiratory Diseases
IX	520-579	Diseases of the Digestive System	Digestive Diseases
X	580-629	Diseases of the Genito-Urinary System	Genito-Urinary Diseases
XI	630-676	Complications of Pregnancy, Childbirth and the Puerperium	Pregnancy Related
XII	680-709	Diseases of the Skin and Subcutaneous Tissue	Skin Diseases
XIII	710-739	Diseases of the Musculo-Skeletal System and Connective Tissue	Musculo-Skeletal Diseases
XIV	740-759	Congenital Anomalies	Congenital Anomalies
XV	760-779	Certain Conditions Originating in the Perinatal Period (Excluding Stillbirths)	Perinatal Conditions
XVI	780-799	Symptoms, Signs and Ill-Defined Conditions	Ill-Defined
E XVII	E800-E999	External Causes, Injury and Poisoning	External Causes

Data Source: Statistics Canada, 1995a

Table 2.13 Example of 4 Digit ICD-9 Coding

ICD-9 Code	Label
153.3	Sigmoid Colon
153	Malignant Neoplasm of Colon
150-159	Malignant Neoplasm of the Digestive Organs and Peritoneum
140-239	Neoplasms
000-E999	All Causes of Death

Data Source: Statistics Canada, 1995a

2.9.1.5 Uncertainty

Alderson (1988) has identified four areas where uncertainties or inaccuracies can arise relating to the reported cause of death:

1. incorrect diagnosis (last attending physician and/or autopsy)
2. incorrect completion of death registration form
3. inaccurate processing and publication of the statistics
4. inaccurate validity of the classification of diseases

The diagnosis relies on the medical training of the individual, the state of medical knowledge and the availability of diagnostic facilities. Different diseases or outcomes vary in the accuracy and consistency of diagnosis. Generally, diagnosis is less precise for older individuals, acute and chronic outcomes can be more or less accurate depending on the disease. Determining the quantitative uncertainty in the diagnosis is very difficult. For mortality, comparisons between clinical and autopsy diagnosis have shown fairly large disagreements. Alderson (1988) summarized five such studies which compared original reported and autopsy verified cause of death. He found only a 50% agreement at the three digit level and an 82% agreement at the chapter level. In Canada, autopsies are performed on approximately 4 out of every 10 deaths, specifically for all fatal injuries and for other sudden or unexpected deaths(Young et al., 1994).

Once a diagnosis is made, the classification form must be completed or encoded properly. There is little information on how much variation exists in completion of the form for the same diagnosis. A survey sent to 97 general practitioners with ten case histories resulted in 7 to 26 different causes of death for the same hypothetical case history (Alderson, 1988). The ease of use and training in using the classification system will influence the reliability of the encoding. By its nature, the classification system assumes that all information entered will be of equal quality, but this is not the case. Lilienfeld and Stolley (1994) showed that some significant differences do occur within a major category when the ICD is revised. However, the difference in the total number of deaths within cardiovascular disease using the ninth ICD compared to the eighth ICD for the same data was only 0.7%.

The final step is the processing and publication of the statistics. Information must be collected in a timely manner for annual publications. For mortality, collection and publication takes approximately two years following the end of a particular year. In Canada, a significant difference existed between the national publication in comparison with the provincial coroner database from which the national data are derived. The

provincial coroner had 13% more accidental deaths, 51% more suicides and 58% more homicides because of delayed transfer of autopsy results (Young et al., 1994). Wilkins (1994) observed that these differences do not effect the total number of deaths.

For mortality, only the underlying cause of death is collected into the national database. Several provinces have started multiple cause coding, which uses information that is already present. This additional information could prove to be valuable for understanding health risks.

As mentioned previously the ICD is a compromise between medical and statistical needs and perspectives, which influences the validity of the classification system. The system must be detailed, easy to use and flexible to allow for new developments.

2.9.2 1993 Evidence

1993 evidence is presented in detail to provide an overview of mortality in Canada. By only providing detailed evidence for one year, the uncertainties associated with comparisons between years are avoided.

2.9.2.1 Cause

As mentioned there are seventeen major categories in the ninth revision of the ICD. The mortality evidence for 1993 is shown in Table 2.14. There is a large difference in the total number of deaths between the different major categories ranging from 15 to 78,894. Two categories, cardiovascular disease and cancer, accounted for 2/3 of all deaths in 1993.

Table 2.14 Mortality by Major Category, 1993

Five of the seventeen categories are dealt with in more detail in Section 2.9.4. In addition to extra information for 1993, trend information (1930-1990) are included for these five categories.

Appendix 1 summarizes the 1993 causes of death in detail beyond that suitable for the main body of this thesis. Subcategories for all seventeen major categories are included. In addition some three digit codes (and in select cases four digit codes) were added. This was done because while these additional subcategories provided useful additional information, in some cases the categories were very broad or were 'other' categories

Table 2.14 Mortality by Major Category, 1993

No.	Shortened Name	Males	Females	Both	% Total
I	Infectious Diseases	2,266	858	3,124	1.5
II	Cancer	30,970	26,211	57,181	27.9
III	Endocrine and Others	2,955	3,425	6,380	3.1
IV	Blood Diseases	373	448	821	0.4
V	Mental Disorders	1,800	2,234	4,034	2.0
VI	Nervous System Diseases	2,586	3,153	5,739	2.8
VII	Cardiovascular Diseases	40,513	38,381	78,894	38.5
VIII	Respiratory Diseases	9,971	8,082	18,053	8.8
IX	Digestive Diseases	3,931	3,624	7,555	3.7
X	Genito-Urinary Diseases	1,607	1,647	3,254	1.6
XI	Pregnancy Related	-	15	15	<0.1
XII	Skin Diseases	67	104	171	0.1
XIII	Musculo-Skeletal Diseases	213	593	806	0.4
XIV	Congenital Anomalies	603	525	1,128	0.6
XV	Perinatal Conditions	615	440	1,055	0.5
XVI	Ill-Defined	1,644	1,488	3,132	1.5
E XVII	External Causes	9,293	4,277	13,570	6.6
	Total	109,407	95,505	204,912	100.0

Data Source: Statistics Canada, 1995a

2.9.2.2 Age

Unfortunately, many popular summaries of information relating to causes of death do not include information on age because of the substantial increase in detail which must be reported. Where one number was used to summarize all ages, ten or more numbers are often required when ages categories are included. This thesis includes divisions by age wherever feasible.

For additional detail, Appendix 2 contains the leading causes of death by age and sex categories for 1993. It provides information for males and females separated into twenty age categories and lists the five leading causes of death.

Figure 2.22 Cause of Death by Age, Males, 1993

Figure 2.23 Cause of Death by Age, Females, 1993

Figures 2.21 and 2.22 show the cause of death by age for males and females in 1993. At ages greater than five, the age categories are shown for every ten years rather than every five years. This was done to simplify presentation. 8 of the 17 major categories from the ICD code were selected with the goal of minimizing the 'other' category (the remaining 9 major categories). The total number of people dying in each category varies tremendously with most deaths occurring in the last three age categories (see Figure 2.7). However, these figures highlight the importance of age when discussing mortality. External causes (fatal injuries), which are the second section from bottom are the leading cause of death for males between the 1-4 to 35-44 age categories, and between 1-4 to 25-34 age categories for females. However, external causes are only ranked fourth in the total number of annual deaths.

2.9.3 Major Causes

Five of the seventeen major categories have been selected for a more detailed analysis. Currently, four of the five are leading causes of death, the fifth, infectious disease was a leading causes of death earlier in the century.

2.9.3.1 1993 Evidence

Major causes of death separated by sex are summarized for the 1993.

Figure 2.22

Cause of Death by Age, Males 1993

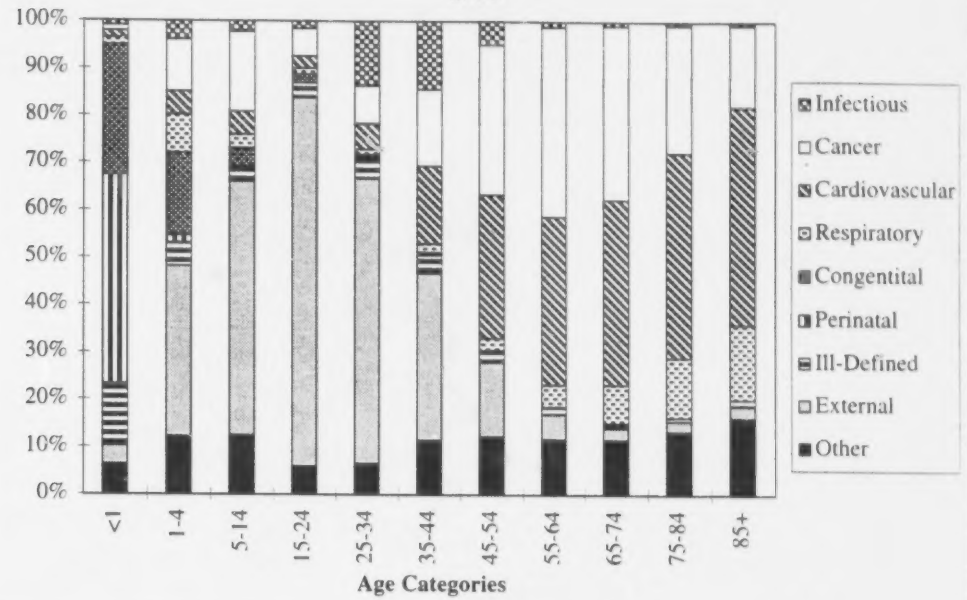
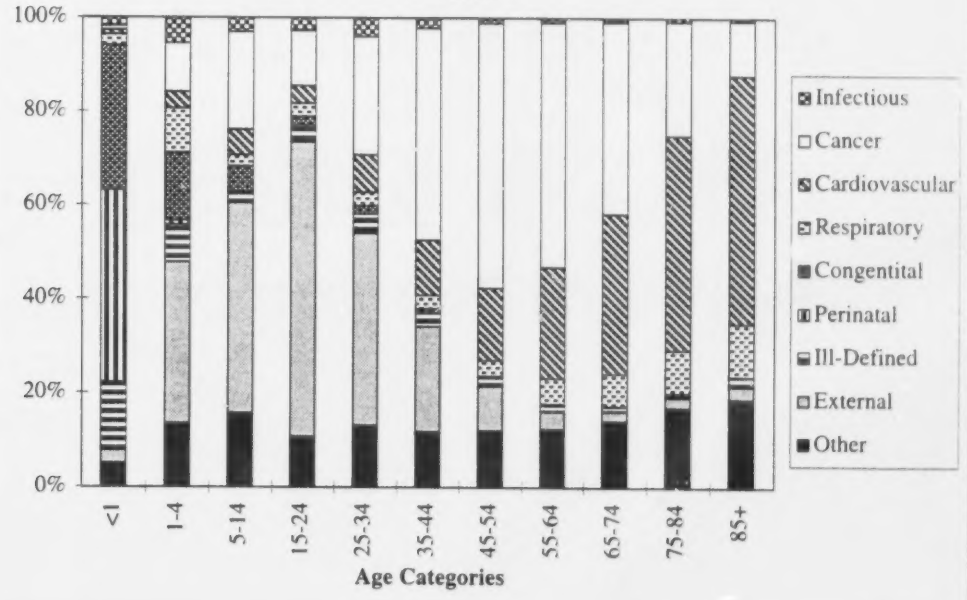


Figure 2.23

Cause of Death by Age, Females 1993



Data Source: Statistics Canada. 1995a

Figure 2.24 Major Causes of Death, Males, 1993

Figure 2.25 Major Causes of Death, Females, 1993

Figures 2.24 and 2.25 show the major causes of death for males and females in 1993. These simple figures highlight the importance of cardiovascular disease and cancer in total annual mortality for both males and females. Males have a significantly higher percentage of deaths from both external causes and infectious diseases compared to females.

2.9.3.2 Trend Evidence

Tracking and comparing mortality between years, especially many years is difficult, but it provides useful insights into how mortality has been changing. We know from life expectancy and age-standardized death rates that people are living longer. However, the question remains how increased life expectancy is related to cause of death.

Figure 2.26 Major Causes Death Rate, Males, 1930-1990

Figure 2.27 Major Causes Death Rate, Females, 1930-1990

Figures 2.26 and 2.27 show the age-standardized death rates for the major causes of death by age for males and females between 1930 and 1990. These figures are probably the most informative figures in the entire thesis. Changes in the significance of the major causes of death for 60 years are shown. For males, cardiovascular disease rose steadily until 1950 and remained level until approximately 1965 when a steady decrease began. For females, cardiovascular disease also rose steadily until 1950 but then started to decrease soon after. Cancer mortality has gradually increased in males since 1930 but has remained constant in females. Infectious diseases dropped significantly for both males and females. Respiratory disease has remained relatively constant as have external causes until a slight decrease started in approximately 1980 for both sexes.

The large drop in the 'other' category until approximately 1960 is partially linked to decreases in infant mortality. The unexpected jump in the 'other' category in 1950 is puzzling. It appears that a consistent increase occurred for all the categories included in the 'other' category in 1950 followed by a huge drop five years later. It does not appear due to a change in classification since none of the 5 major causes mirrors the jump.

The next five sections (2.9.3.3 - 2.9.3.7) focus on each of the five major causes of death. Each section has been organized into two subsections, one on 1993 evidence and the other trend evidence from 1930 to 1990. For each 1993 subsection, 4 standard figures have

Figure 2.24

Major Causes of Death, Males
1993

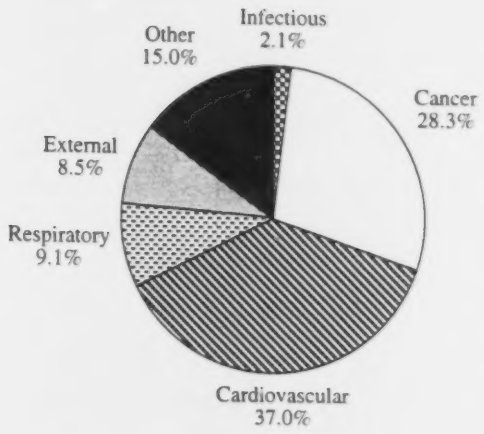
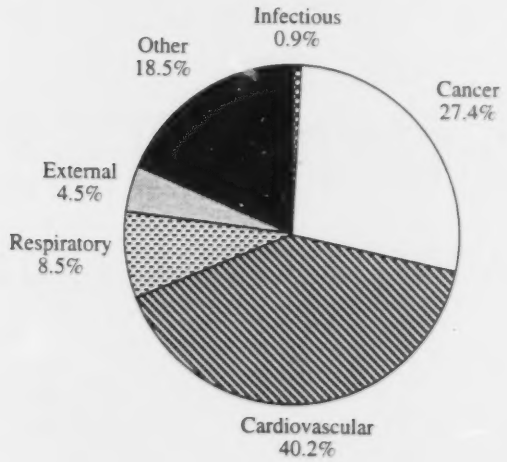


Figure 2.25

Major Causes of Death, Females
1993



Data Source: Statistics Canada, 1995a

Figure 2.26

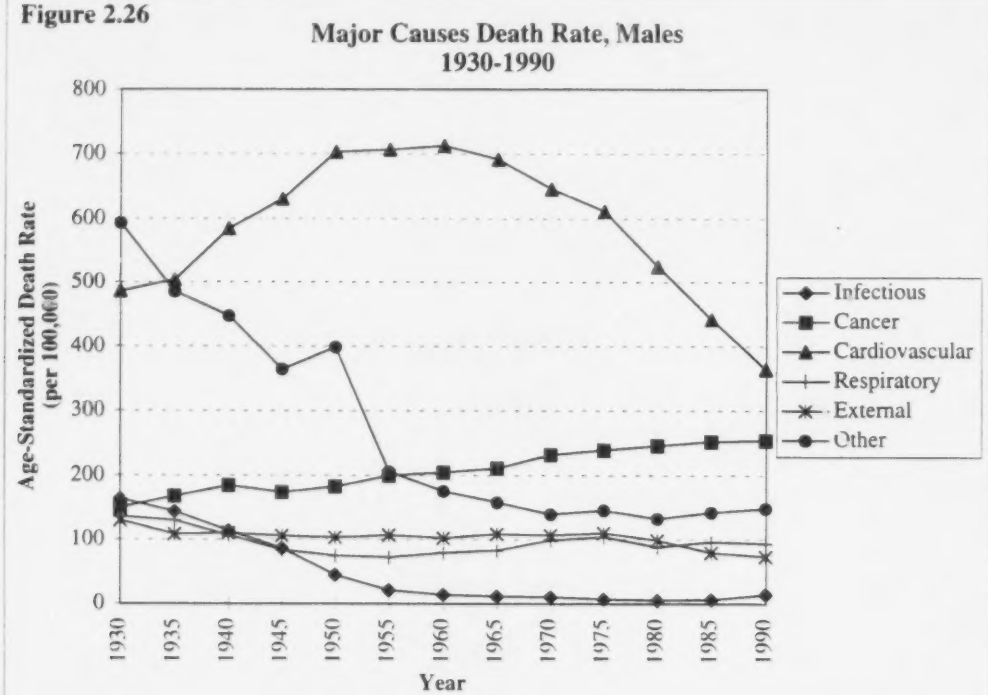
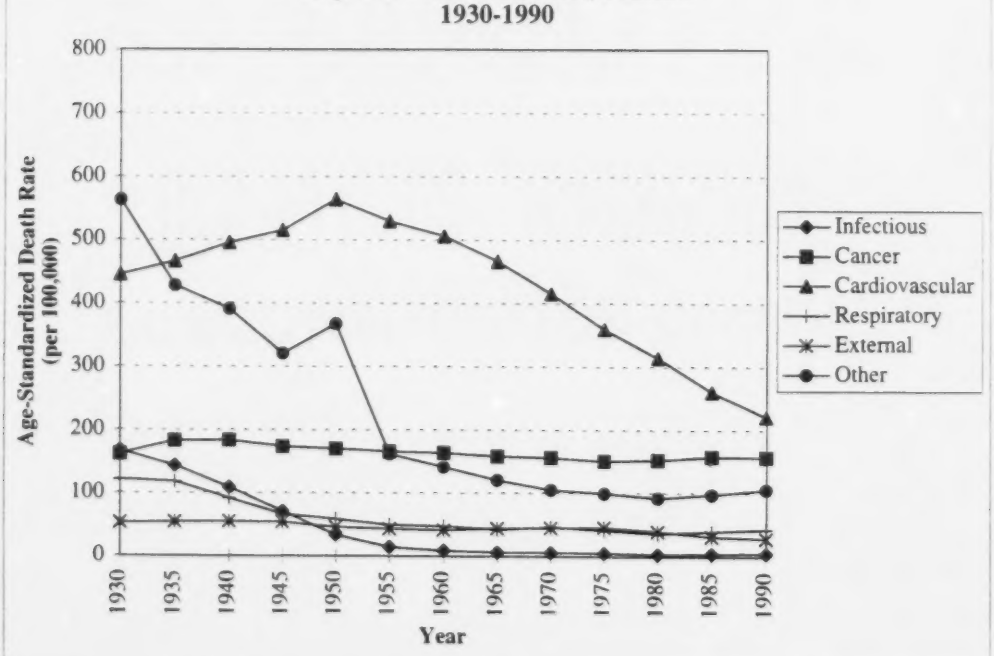


Figure 2.27



Data Source: see Table 2.4

been prepared and for each trend subsection, and for each trend subsection, 2 standard figures have been prepared. These standard figures are introduced below:

First - Death by Age, Males, 1993
Second - Death Rate by Age, Males, 1993

Third - Death by Age, Females, 1993
Fourth - Death Rate by Age, Females, 1993

Fifth - Death Rate, 1930-1990

Sixth - Death Rate by Age, Both, 1930-1990

The first and second figure are presented together on the same page because they are meant to be used together. The first figure shows the total number of deaths in 1993 for males from the three or four leading causes of death from within each of the five major causes of death. This evidence is shown for twenty age categories. The second figure shows the death rate which uses the evidence from the first figure divided by the population in each age category. The three or four leading causes of death for each major cause of death were selected from the numbers in Appendix 1. The three digit ICD-9 for each of the three or four leading causes of death are provided so they can located in Appendix 1 . The first figure, showing the total number of deaths, is an arithmetic scale and has its vertical set by the data (varies from 100 to 3,000). The second figure, showing the death rate, is a logarithmic scale and has its vertical fixed (from 0.1 to 100,000). The first and second figure show useful information that is enhanced by each other. The first figure is easier to read because of its arithmetic scale but because there is a large difference in the population in each age category the second figure, though harder to interpret is able to more clearly display difference in mortality between age categories.

The third and fourth figure are similar to the first and second except they are for females instead of males. The same three or four leading causes of death are the same in each of the five major causes of death except for cancer where one of leading of causes of cancer death for males, prostate cancer, is replaced with breast cancer for females.

The five and sixth figure are not meant to be read together like the first four figures. The fifth figure simply combines Figure 2.26 and 2.27 (Major Causes Death Rate, Male and

Female) into one figure for that specific cause of death. This age-standardized death rate shows the change in the death rate over time and the difference between sexes.

The sixth figure takes four years at twenty years intervals (1930, 1950, 1970 and 1990) and compares the death rate by age. Age-standardization is not required because the age categories are used. These figures highlight at what age the most significant changes in the death rate have occurred. Both sexes are combined because on a log scale the differences are hard to distinguish and the fifth figure provides insight into the overall difference in the death rate between sexes.

2.9.3.2.1 Method for Trend Evidence

This subsection will review some of the difficulties encountered in preparing the figures for the trend evidence related to changes in the classification system. Table 2.15 summarizes how the classification system has changed between 1930 and 1990 including when provinces and territories were included in the totals.

Table 2.15 Changes to Classification System, 1930-1990

Canada has been using the ICD for causes of death since 1921 when it was based on the ICD-3 (Taylor, 1992). However, the first mention of the ICD in the published reports used in this thesis was for 1945 when the ICD-5 was being used. Considering the dates new ICD revisions were introduced, 1930 information probably used the ICD-3, 1935 the ICD-4 and 1940 the ICD-4 or ICD-5.

Alderson (1988) reviewed the major changes for the 3rd to 9th ICD revisions. The only major change that affected this thesis related to cerebrovascular diseases (stroke). Cerebrovascular diseases was in the 'Diseases of the Nervous System' major category until the ICD-8 when it was moved into 'circulatory diseases' (Cardiovascular Diseases). This meant that numbers in the cardiovascular disease category reported fewer deaths between 1930 and 1965. This difference was significant since cerebrovascular diseases accounted for more than 1/4 of deaths when added to the cardiovascular disease category. Therefore, cerebrovascular diseases were extracted from the nervous system category and placed in cardiovascular disease category for 1930-1965.

Table 2.15 Changes to Classification System, 1930-1990

Year	ICD No.	No. Families	Comments
1930	?	XV	Newfoundland not included Yukon and NWT in appendix Neoplasms not its own family
1935	?	XVIII	Newfoundland not included Yukon and NWT in appendix
1940	?	XVIII	Newfoundland not included Yukon and NWT in appendix
1945	5	XVIII	Newfoundland not included Yukon and NWT in appendix
1950	6	XVII	Yukon and NWT in appendix
1955	6	XVII	Yukon and NWT in appendix
1960	7	XVII	
1965	7	XVII	
1970	8	XVII	Cerebrovascular disease moved from nervous system to circulatory system
1975	8	XVII	
1981	9	XVII	
1985	9	XVII	
1990	9	XVII	

Data Source: see Table 2.4

A less significant difficulty occurred in 1930 when cancer was part of major category named 'General Diseases Not Included in Class I'. Cancer was list no. 43-49 which did not include 'benign tumours and tumours not listed as malignant', list no. 50 and 'leukaemia, lymphadenoma', list no. 65. These extra 560 deaths represented 6% of the reported 9,273 cancer deaths. This was relatively small and the extra deaths were not included. For 1935, 1940 and 1945 'leukaemia and aleukaemia' were not included with cancer. The total number of deaths for each year from this cause was 362, 484 and 415 respectively which was approximately 3% of all cancer deaths each year. These extra deaths were also not included.

2.9.3.3 Infectious Disease

In 1993, infectious disease was the cause of death for 2.1% of males and 0.9% of females. While infectious diseases are currently no longer a leading annual cause of death they were earlier in the century. The two infectious diseases of current concern in Canada are AIDS (HIV infection) and tuberculosis (on the rise). However, the Center for Disease Control (CDC) has identified several emerging infectious disease threats in the U.S. (CDC, 1994):

- E. coli O157:H7 disease
- Cryptosporidiosis
- Coccidioidomycosis
- Multidrug-resistant pneumococcal disease
- Vancomycin-resistant enterococcal infections
- Influenza A/Beijing/32/92
- Hantavirus infections

Another example of infectious disease outbreaks occurred in Canada with meningococcal disease which killed several adolescents and young adults in 1991 and 1992 (Shah, 1994).

2.9.3.3.1 1993 Evidence

Infectious deaths separated by sex are summarized for the 1993.

The three sub-categories of infectious disease considered in more detail are:

- Tuberculosis (ICD-9: 010-018, 137)

- Septicaemia (ICD-9: 038)
- HIV infection (ICD-9: 042-044)

Figure 2.28 Infectious Deaths by Age, Males, 1993
Figure 2.29 Infectious Death Rate by Age, Males, 1993
Figures 2.28 and 2.29 show the number of infectious deaths by age and the infectious death rate by age for males in 1993. HIV infection has made a significant impact on male mortality. Considering that it can take many years following the initial HIV infection to die, the fact that those dying are still relatively young stresses the impact of HIV infection on the young. Deaths from HIV infection in males is the only cause of death of all those summarized in this thesis where the death rate decreases with increasing age. While tuberculosis kills a relatively small number of people annually, it's still a priority from a public health perspective.

Figure 2.30 Infectious Deaths by Age, Females, 1993
Figure 2.31 Infectious Death Rate by Age, Females, 1993
Figures 2.30 and 2.31 show the number of infectious deaths by age and the infectious death rate by age for females in 1993. When comparing the male infectious deaths by age (Figure 2.28) and females infectious deaths by age (Figure 2.30), note that the number of deaths on the vertical axis are different. Unlike males, HIV infection for females has had only a small impact on mortality to date. The death rates by age for septicaemia and tuberculosis are similar for males and females.

2.9.3.3.2 Trend Evidence

Infectious deaths are summarized for 1930 to 1990.

Figure 2.32 Infectious Death Rate, 1930-1990
Figures 2.32 shows the infectious death rate for males and females between 1930 and 1990. An enormous decline in infectious deaths, which started before 1930, continued until approximately 1955 when a more gradual decline followed. The increase between 1985 and 1990 in males is due to HIV infection. After 1940 females have had a lower mortality rate from infectious disease than males.

Figure 2.28

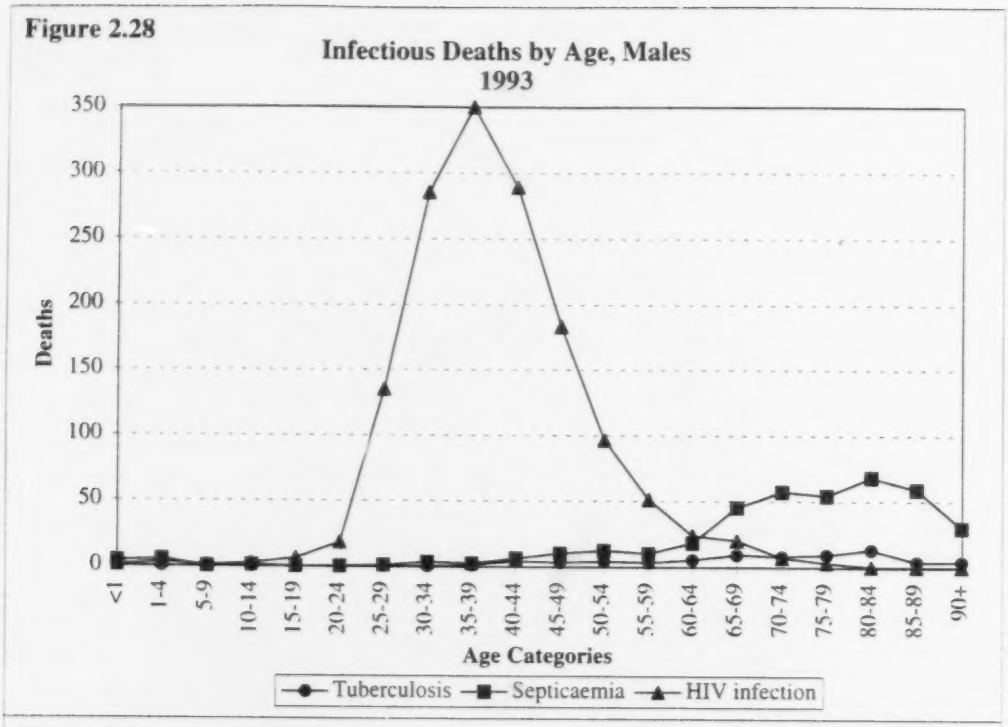
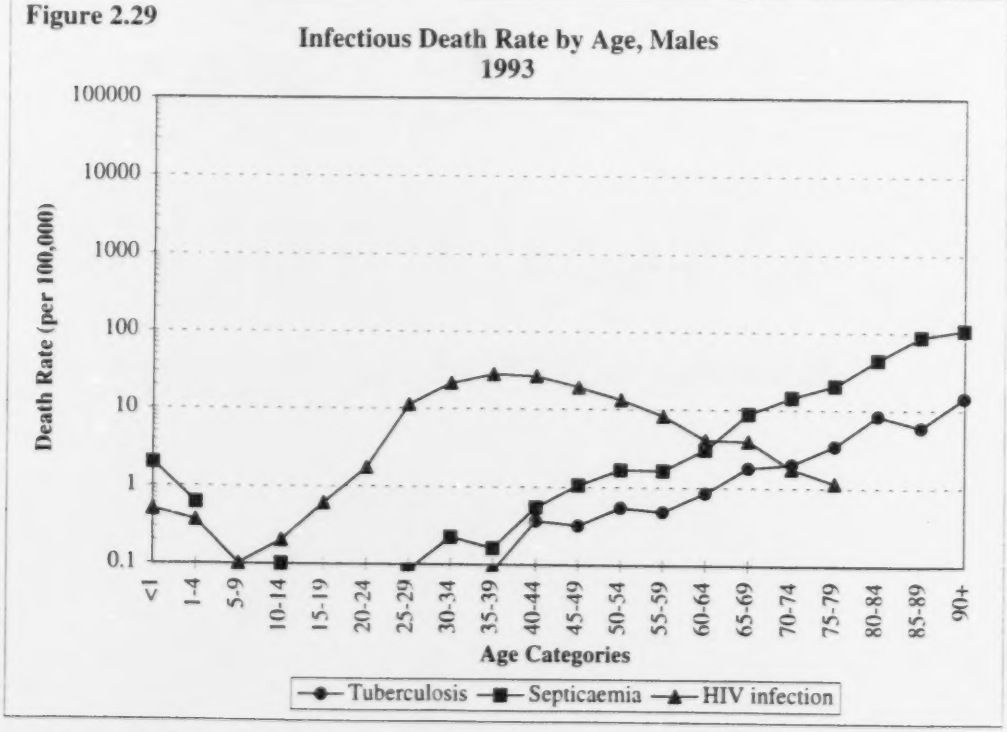


Figure 2.29



Data Source: Statistics Canada. 1995a

Figure 2.30

Infectious Deaths by Age, Females 1993

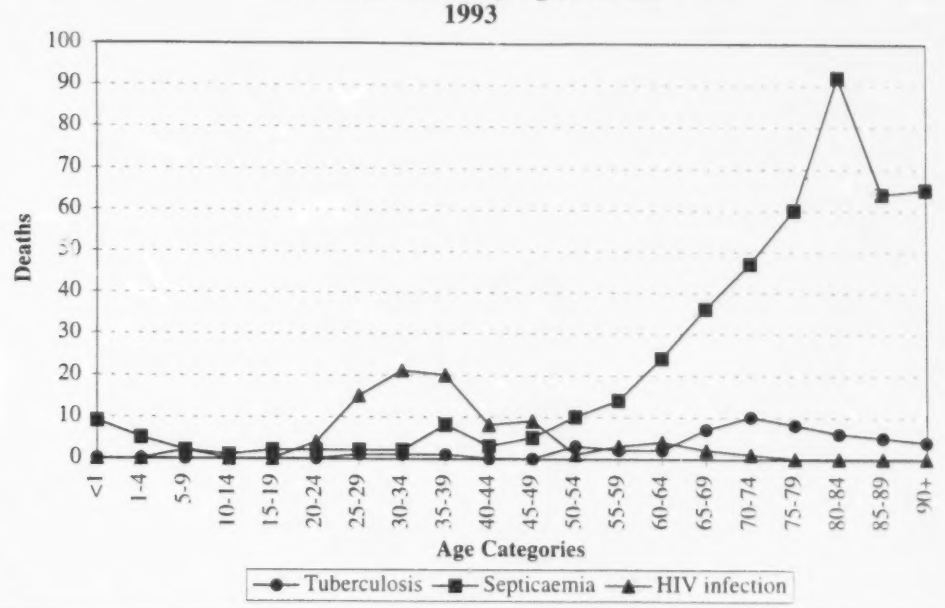
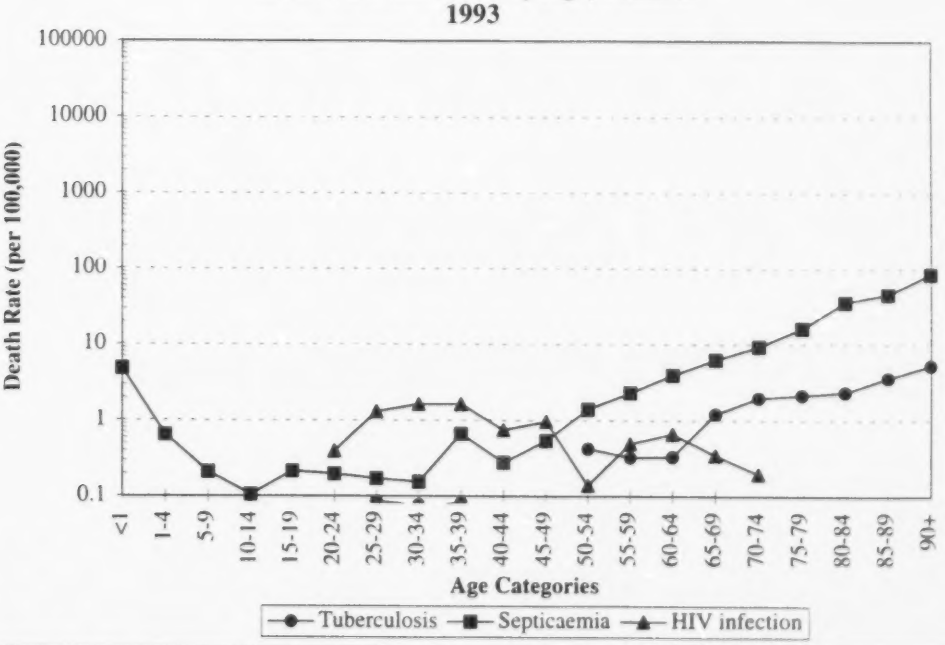


Figure 2.31

Infectious Death Rate by Age, Females 1993



Data Source: Statistics Canada, 1995a

Figure 2.32

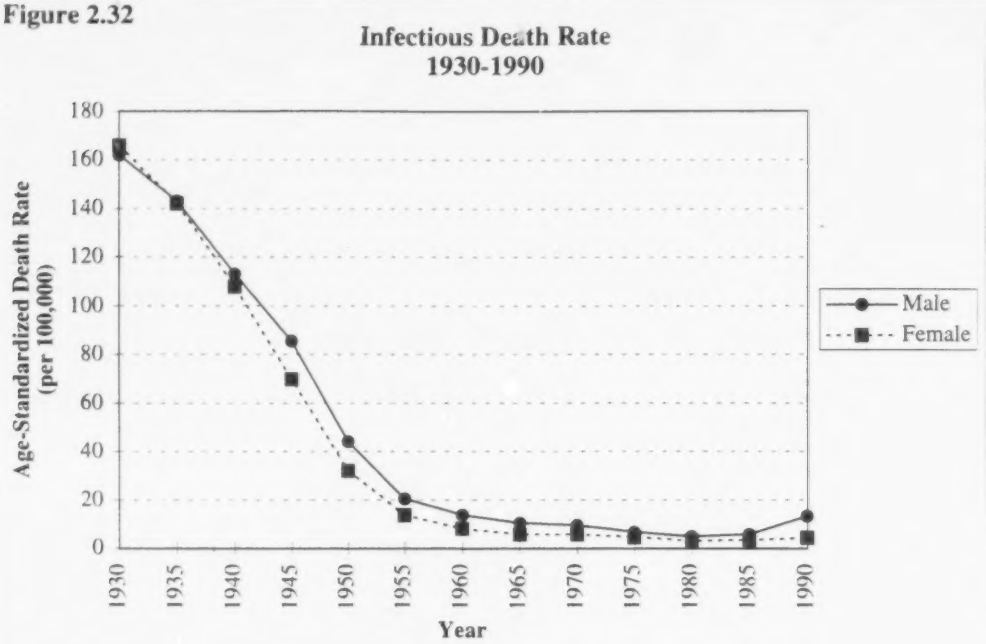
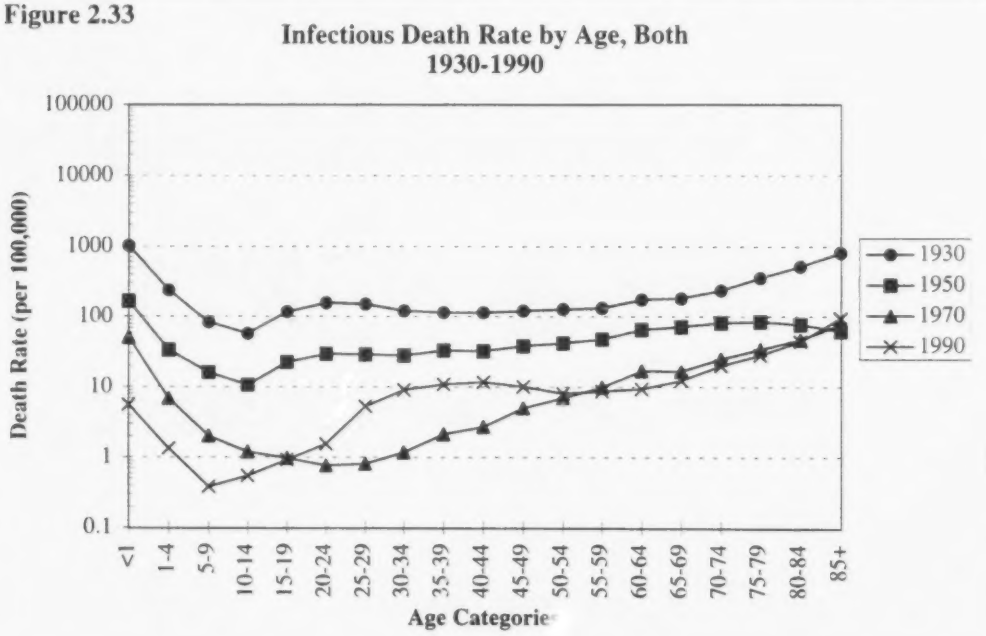


Figure 2.33



Data Source: see Table 2.4

Figure 2.33 Infectious Death Rate by Age, Both Sexes, 1930-1990

Figures 2.33 shows the infectious death rate by age for males and females combined between 1930 and 1990. Significant drops in the infectious death rate have occurred in most age categories. For example in the <1 age category, steady drops took place and the death rate fell from approximately 1,000 to 5 deaths per 100,000 between 1930 and 1990. The increase in death rate between 1970 and 1990 between age categories 20-24 and 55-59 is because of HIV infection.

2.9.3.4 Cancer

Cancer is a general term for neoplasms which are abnormal tissue that grows by cellular proliferation more rapidly than normal and continues to grow after the stimuli that initiated the new growth cease (Stedman's Medical Dictionary, 1995). In 1993, cancer was the cause of death for 28% of males and 27% of females.

There are over 100 different types of cancer which often have significantly different properties. One important measure for individual types cancers is the relative survival rate. This can be determined by measuring the percentage of people surviving five years past diagnosis or more indirectly by comparing the number of deaths to new cases in a year. The higher the ratio of deaths to new cases, the lower the relative survival. Some ratios for individual types of cancer include (National Cancer Institute of Canada, 1996)

- pancreas - 1.02
- lung - 0.85
- stomach - 0.67
- female breast - 0.28
- prostate - 0.23
- testis - 0.03

Since cancer incidence is such a significant factor in relation to individual types of cancer, a summary of incidence data has been included in the trend section. A more detailed breakdown of cancer is beyond the scope of this thesis but the annual publication Canadian Cancer Statistics provides a more detailed breakdown of the various types of cancer by site and also includes a section on childhood cancer.

2.9.3.4.1 1993 Evidence

Cancer deaths separated by sex are summarized for the 1993.

The four sub-categories of cancer considered in more detail are:

- Colon (ICD-9: 153)
- Pancreas (ICD-9: 157)
- Lung (ICD-9: 162 - includes trachea and bronchus)
- Prostate (ICD-9: 185) - Males only
- Breast (ICD-9: 174) - Females only

Figure 2.34 Cancer Deaths by Age, Males, 1993
Figure 2.35 Cancer Death Rate by Age, Males, 1993

Figures 2.34 and 2.35 show the number of cancer deaths by age and the cancer death rate by age for males in 1993. Lung cancer is the most significant of cancers in terms of total deaths and the age at which deaths first start occurring. Prostate cancer, the second leading cause of cancer deaths starts its rise approximately 15 years later than lung cancer. Virtually no cancer deaths occur in the young from these particular cancers, other types are more prevalent (e.g. leukemia, brain and spinal cancers).

Figure 2.36 Cancer Deaths by Age, Females, 1993
Figure 2.37 Cancer Death Rate by Age, Females, 1993

Figures 2.36 and 2.37 show the number of cancer deaths by age and the cancer death rate by age for females in 1993. When comparing the male cancer deaths by age (Figure 2.34) and females cancer deaths by age (Figure 2.36), note that the number of deaths on the vertical axis are different. Lung cancer for females, which surpassed breast cancer in number of annual deaths in 1993, has a nearly identical age distribution compared to males except the numbers are approximately half. Breast cancer mortality in females occurs earlier in life than others types of cancer.

2.9.3.4.2 Trend Evidence

Cancer deaths are summarized for 1930 to 1990. Cancer incidence information is also included.

Figure 2.34

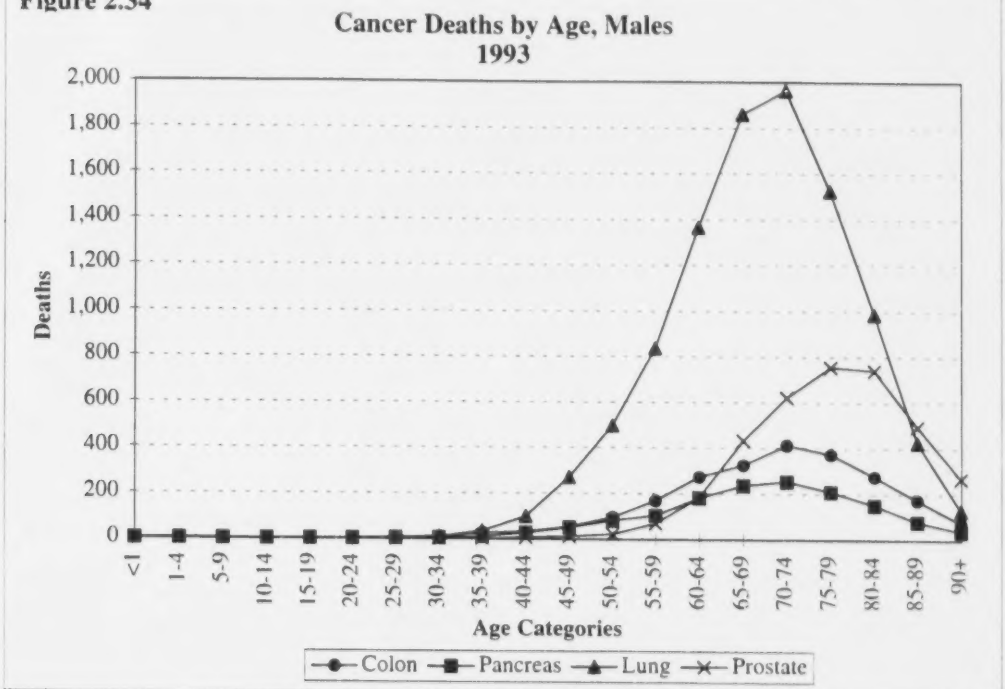
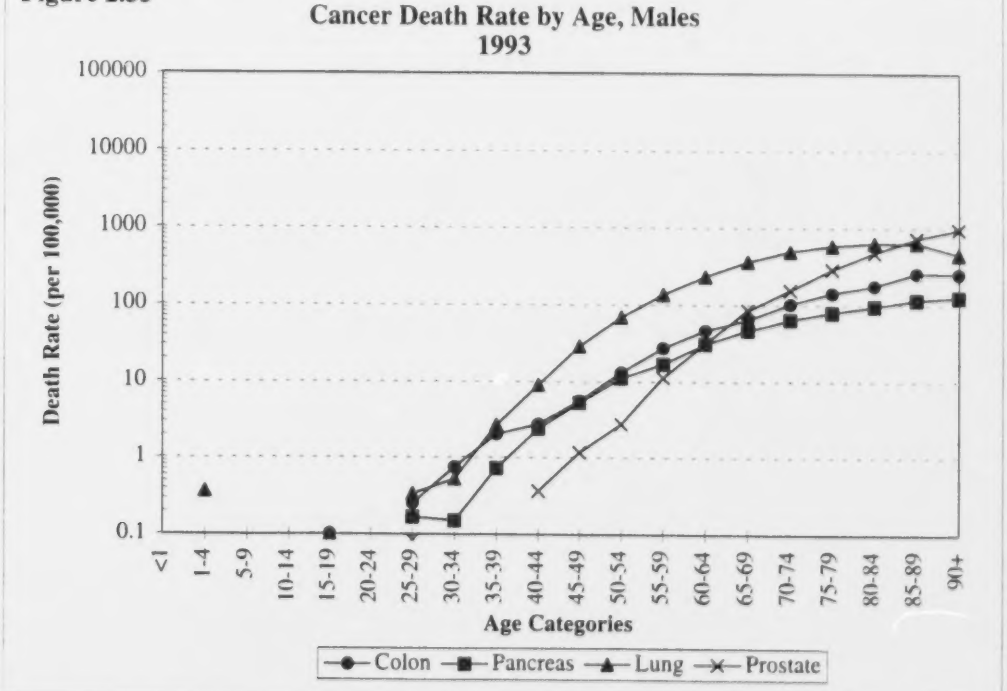


Figure 2.35



Data Source: Statistics Canada, 1995a

Figure 2.36

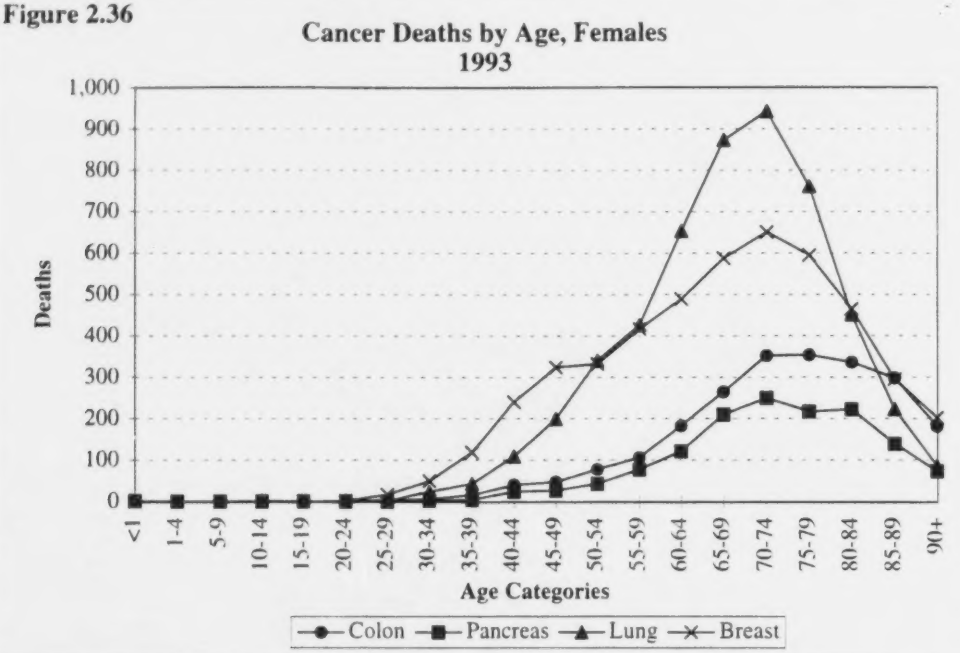
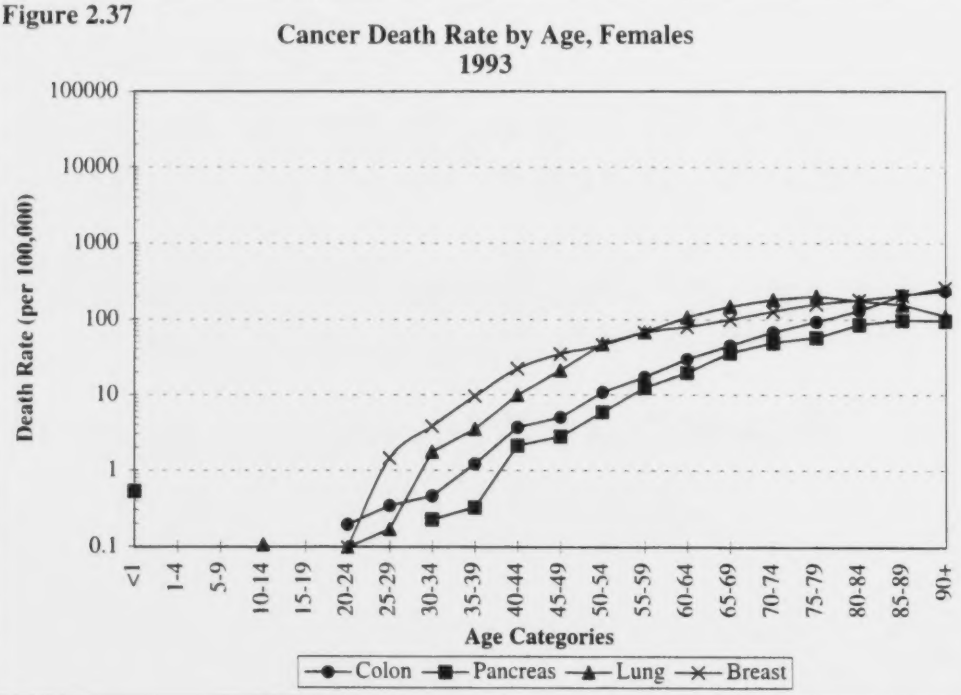


Figure 2.37



Data Source: Statistics Canada, 1995a

Figure 2.38 Cancer Death Rate, 1930-1990

Figures 2.38 shows the cancer death rate for males and females between 1930 and 1990. For males, the cancer death rate has been steadily increasing until 1980 with a more gradual increase since. For females, the cancer death rate has remained relatively constant.

Figure 2.39 Cancer Death Rate by Age, Both Sexes, 1930-1990

Figures 2.39 shows the cancer death rate by age for males and females combined between 1930 and 1990. The lower cancer rates in the young in 1930 is probability due to misclassification resulting from diagnosis and the coding practices at the time. The lower rates in 1990, however, is likely a reflection of decreases in mortality.

Figure 2.40 Age-Standardized Incidence Rates for Selected Cancer Sites, Males, 1969-1996

Figure 2.41 Age-Standardized Mortality Rates for Selected Cancer Sites, Males, 1969-1996

Figures 2.40 and 2.41 show the incidence and mortality cancer death rates for males between 1969 and 1996. The incidence rates are provided to highlight the large differences in the ratio of deaths to new cases which was discussed at the beginning of this section on cancer. While prostate cancer is currently the most common form of cancer in males (Figure 2.40) lung cancer remains the leading cause of death from cancer (Figure 2.41). Some of the risk factors associated with specific types cancers are discussed in the indirect evidence and inference section.

Figure 2.42 Age-Standardized Incidence Rates for Selected Cancer Sites, Females, 1969-1996

Figure 2.43 Age-Standardized Mortality Rates for Selected Cancer Sites, Females, 1969-1996

Figures 2.42 and 2.43 show the incidence and mortality cancer death rates for females between 1969 and 1996. The incidence rates are provided to highlight the large differences in the ratio of deaths to new cases which was discussed at the beginning of this section on cancer. Breast cancer is the most common form of cancer in females. One of the most significant trends in females are the significant increases in the incidence and the mortality from lung cancer. Some of the risk factors associated with specific types cancers are discussed in the indirect evidence and inference section.

Figure 2.38

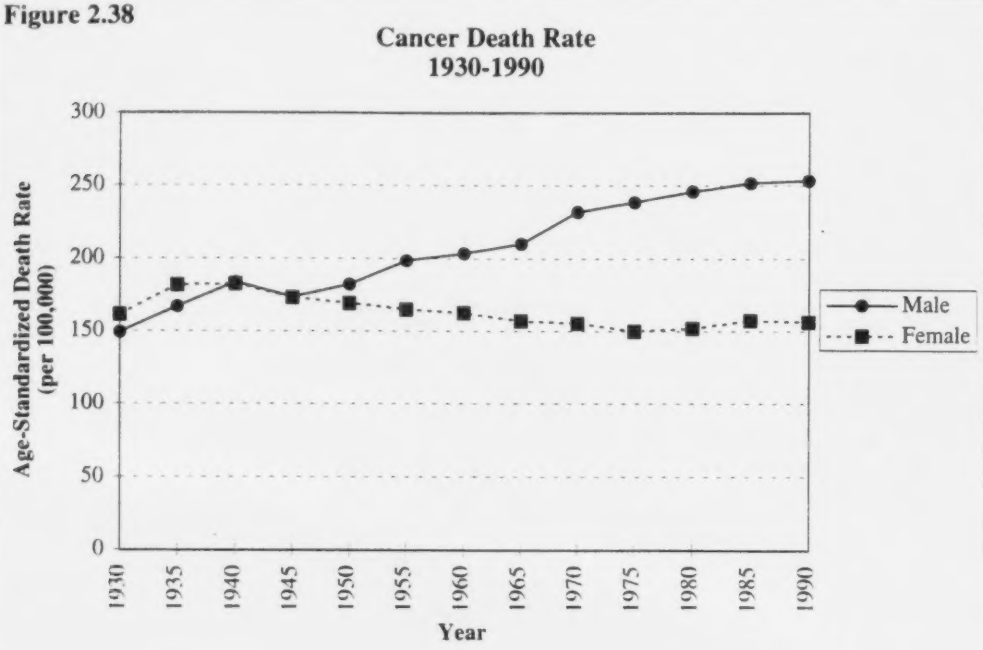
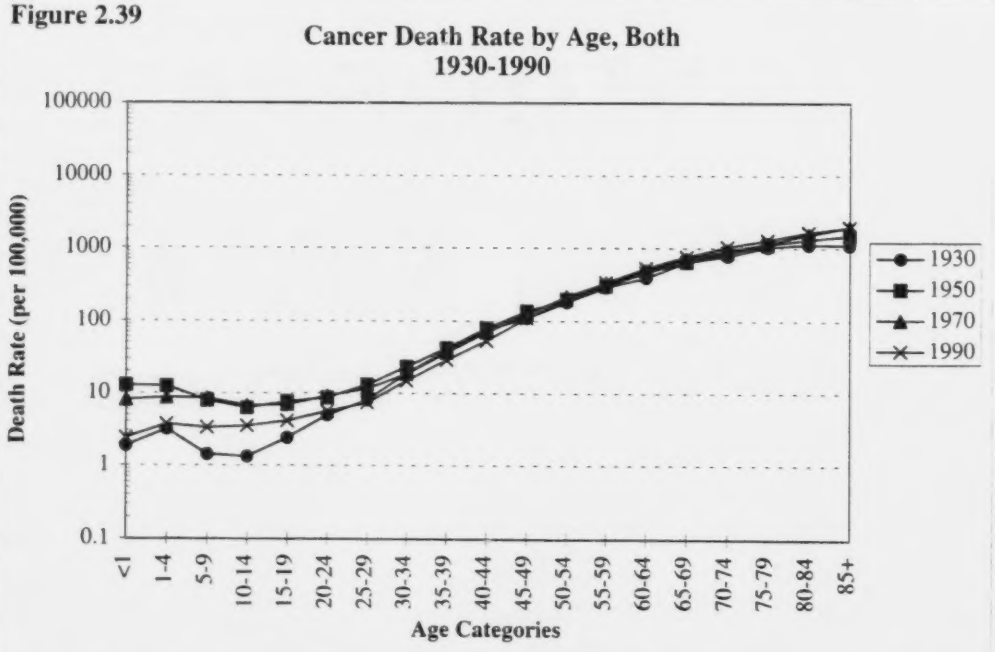


Figure 2.39



Data Source: see Table 2.4

Figure 2.40 Age-Standardized Incidence Rates for Selected Cancer Sites, Males, 1969-1995

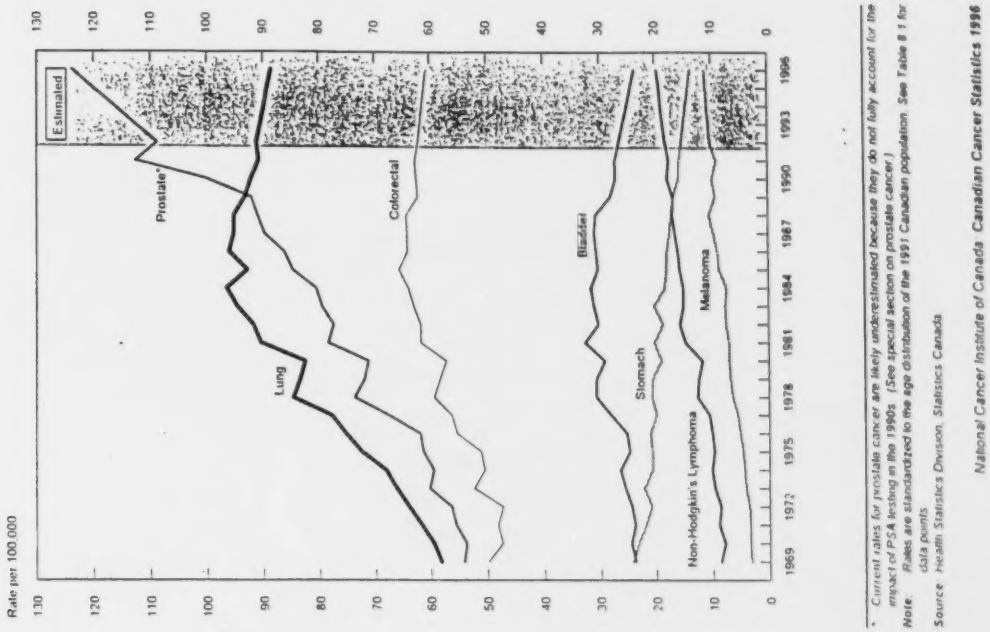

Rate per 100,000
Estimated
Prostate*
Lung
Colorectal
Bladder
Stomach
Non-Hodgkin's Lymphoma
Melanoma
1969 1972 1975 1978 1981 1984 1987 1990 1993 1996
* Current rates for prostate cancer are likely underestimated because they do not fully account for the impact of PSA testing in the 1990s (See special section on prostate cancer.)
Note: Rates are standardized to the age distribution of the 1991 Canadian population. See Table B.1 for data points
Source: Health Statistics Division, Statistics Canada
National Cancer Institute of Canada Canadian Cancer Statistics 1996

Figure 2.41 Age-Standardized Mortality Rates for Selected Cancer Sites, Males, 1969-1995

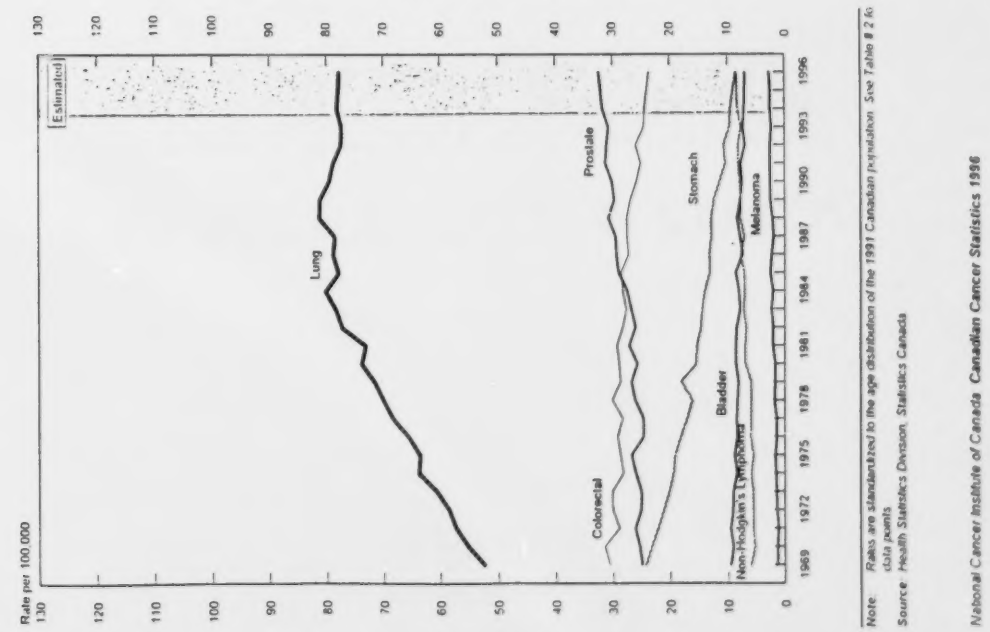
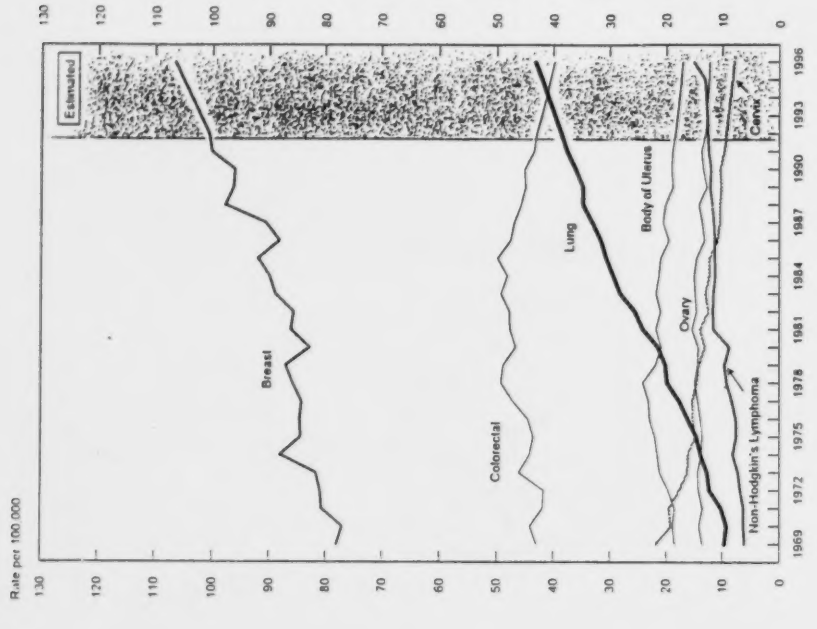

Rate per 100,000
Estimated
Lung
Prostate
Stomach
Colorectal
Bladder
Melanoma
Non-Hodgkin's Lymphoma
1969 1972 1975 1978 1981 1984 1987 1990 1993 1996
Note: Rates are standardized to the age distribution of the 1991 Canadian population. See Table B.2 for data points
Source: Health Statistics Division, Statistics Canada
National Cancer Institute of Canada Canadian Cancer Statistics 1996

Figure 2.42 Age-Standardized Incidence Rates for Selected Cancer Sites, Females, 1969-1995

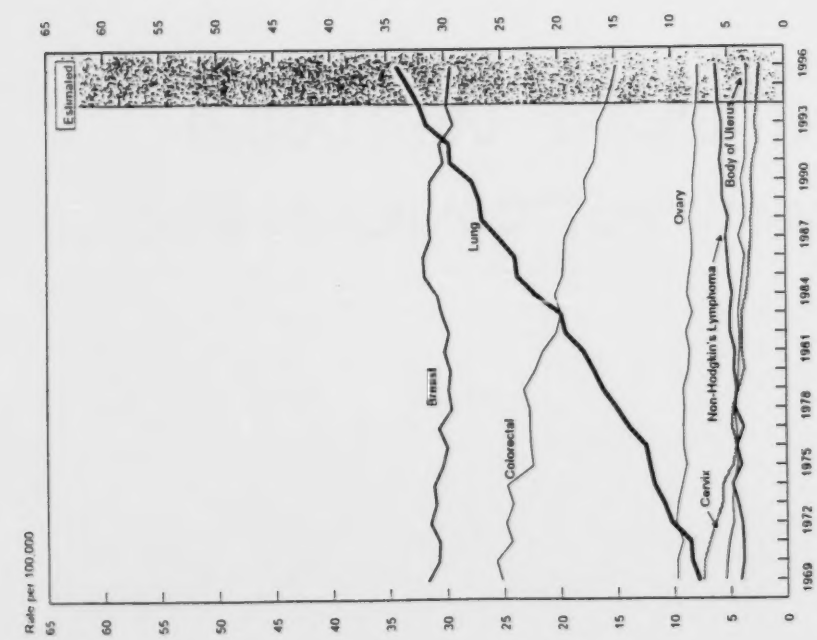


Note: Rates are standardized to the age distribution of the 1991 Canadian population. See Table 9.1 for data points.

Source: Health Statistics Division, Statistics Canada

National Cancer Institute of Canada. Canadian Cancer Statistics 1996

Figure 2.43 Age-Standardized Mortality Rates for Selected Cancer Sites, Females, 1969-1995



Note: Rates are standardized to the age distribution of the 1991 Canadian population. See Table 9.2 for data points.

Source: Health Statistics Division, Statistics Canada

National Cancer Institute of Canada. Canadian Cancer Statistics 1996

2.9.3.5 Cardiovascular Disease

Cardiovascular disease includes heart disease and stroke (cerebrovascular disease). Cardiovascular disease is also known as circulatory disease. In 1993, cardiovascular disease was the cause of death for 37% of males and 40% of females. Most cardiovascular disease is a result of atherosclerosis which refers to the buildup of lipid deposits in the arteries.

2.9.3.5.1 1993 Evidence

Cardiovascular deaths separated by sex are summarized for the 1993.

The four sub-categories of cardiovascular disease considered in more detail are:

- AMI (ICD-9: 410) - Acute Myocardial Infarction - the medical term for a heart attack
- Other IHD (ICD-9: 414) - Other forms of Ischaemic Heart Disease
- Other Heart (ICD-9: 420-429) - Other forms of Heart Disease
- Stroke (ICD-9: 430-438) - Cerebrovascular Disease

Figure 2.44 Cardiovascular Deaths by Age, Males, 1993
Figure 2.45 Cardiovascular Death Rate by Age, Males, 1993
Figures 2.44 and 2.45 show the number of cardiovascular deaths by age and the cardiovascular death rate by age for males in 1993. Beginning around the age of 40, cardiovascular deaths increase significantly and exponentially with age. Deaths from heart attacks (acute myocardial infarction) are the most significant and because they are rapid and kill more people at earlier ages than other forms of heart disease. The sharp drop in the number of deaths for the last two age categories in Figure 2.44 occurs because the majority of males have already died.

Figure 2.46 Cardiovascular Deaths by Age, Females, 1993
Figure 2.47 Cardiovascular Death Rate by Age, Females, 1993
Figures 2.46 and 2.47 show the number of cardiovascular deaths by age and the cardiovascular death rate by age for females in 1993. Overall most types of deaths from cardiovascular disease in females are shifted approximately 10 to 20 years later in life than males.

Figure 2.44

Cardiovascular Deaths by Age, Males 1993

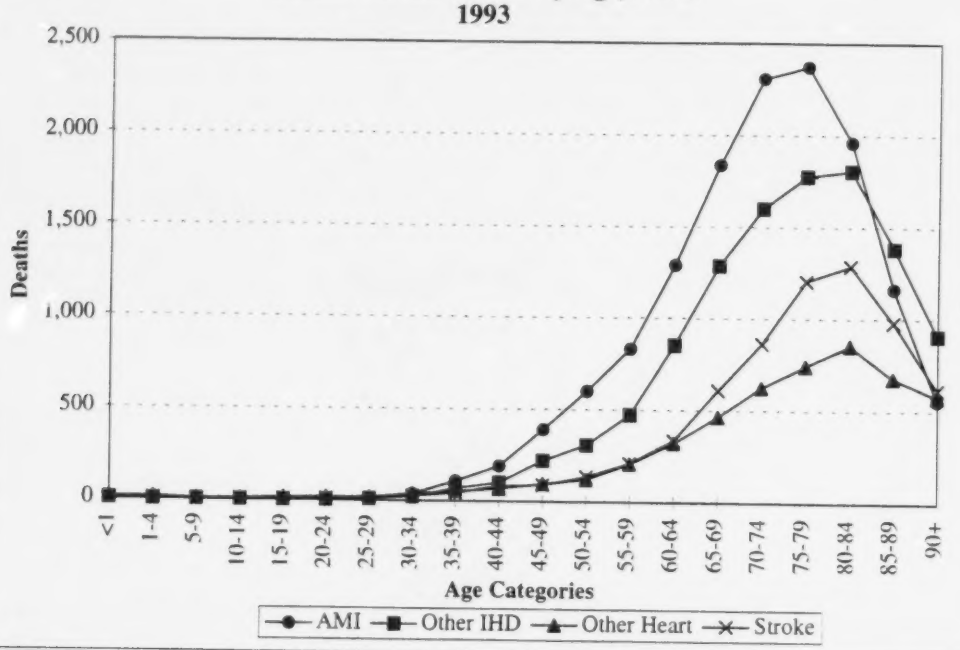
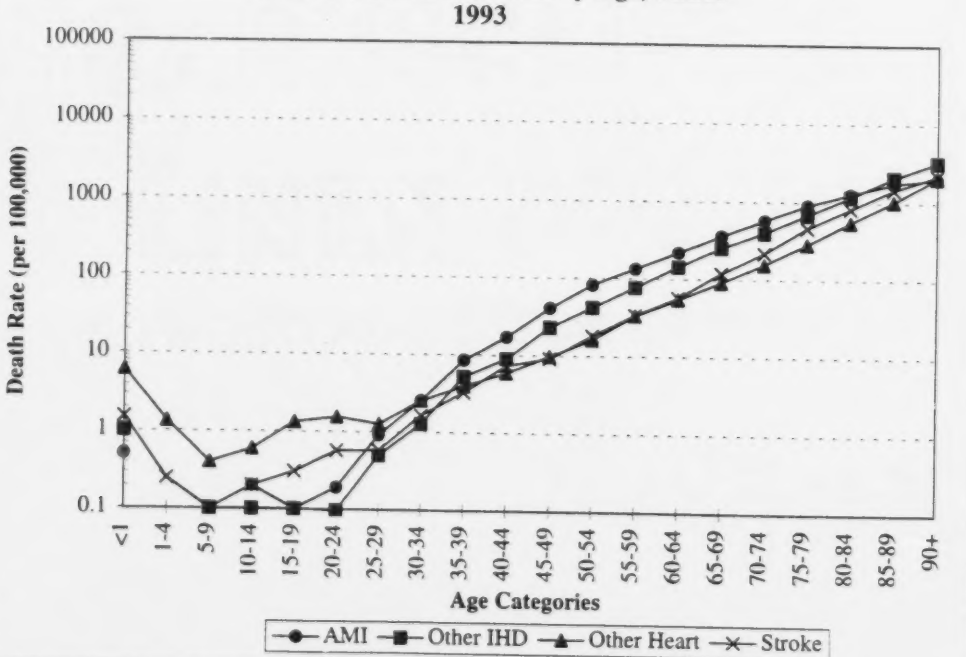


Figure 2.45

Cardiovascular Death Rate by Age, Males 1993



Data Source: Statistics Canada, 1995a

Figure 2.46

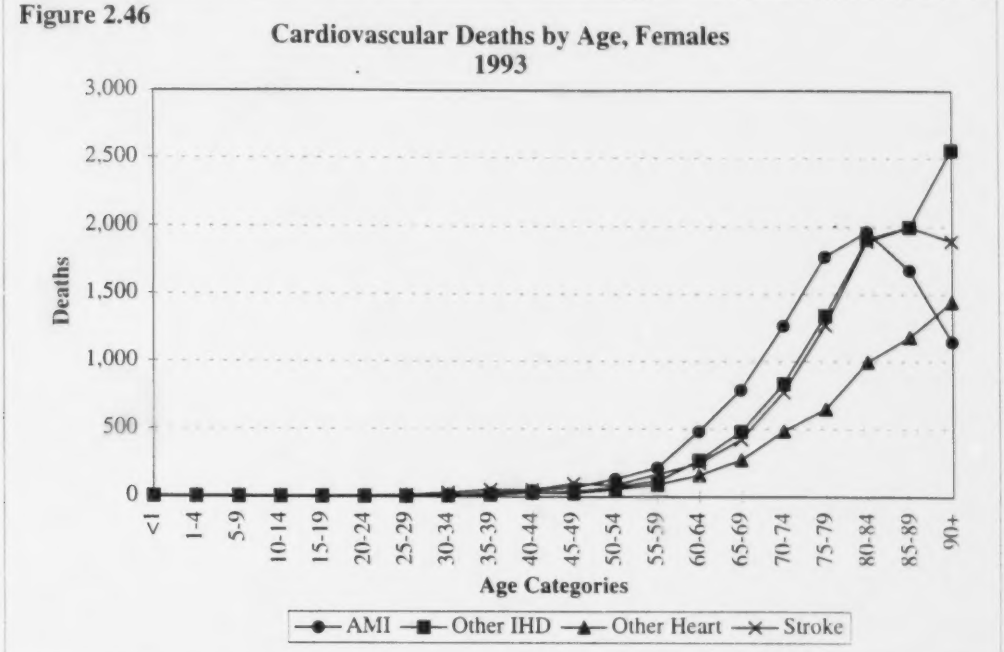
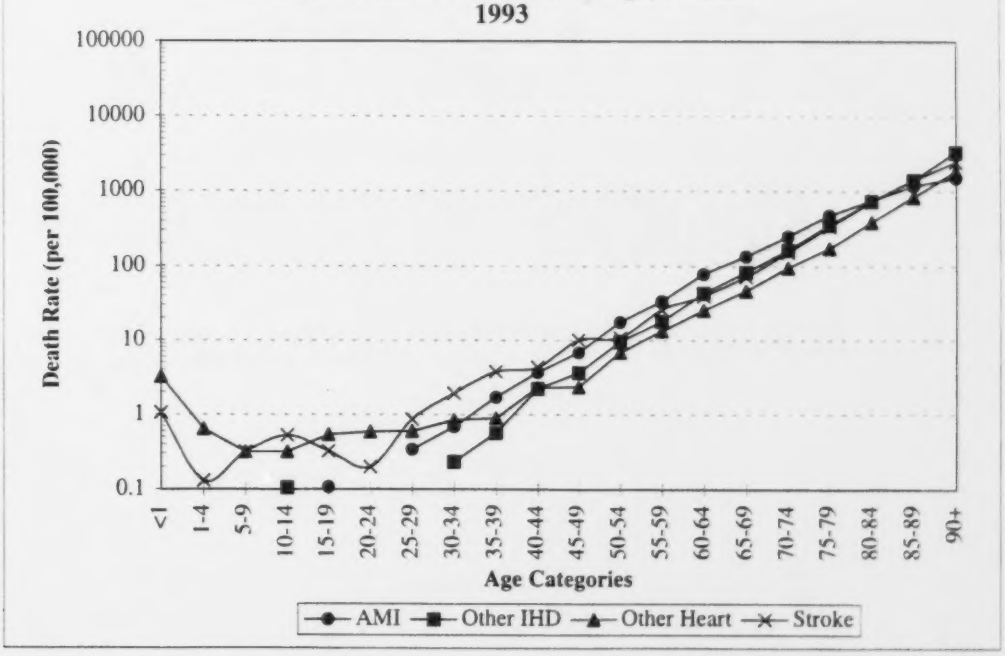


Figure 2.47



Data Source: Statistics Canada, 1995a

2.9.3.5.2 Trend Evidence

Cardiovascular deaths are summarized for 1930 to 1990.

Figure 2.48 Cardiovascular Death Rate, 1930-1990

Figure 2.48 shows the cardiovascular death rate for males and females between 1930 and 1990. This figure highlights the significant declines in morality since 1965 in males and since 1955 in females. The widening of the gap in death rates between sexes from cardiovascular disease occurred primarily between 1930 to 1965. Since 1975 the gap in death rates has been slowly closing.

Figure 2.49 Cardiovascular Death Rate by Age, Both, 1930-1990

Figure 2.49 shows the cardiovascular death rate by age for males and females combined between 1930 and 1990. Some significant declines in the death rate in children and young adults (ages 5 to 24) have occurred. However, since relatively few people die from cardiovascular diseases at these young ages, the net reduction to morality is small. A more significant reduction in mortality has occurred in most age categories between 1970 and 1990.

2.9.3.6 Respiratory Disease

Respiratory disease is associated with the lungs and airways. In this thesis (and in the ICD) respiratory disease are non-cancer related disease. In 1993, respiratory disease was the cause of death for 9.1% of males and 8.5% of females.

2.9.3.6.1 1993 Evidence

Respiratory deaths separated by sex are summarized for the 1993.

The four sub-categories of respiratory disease considered in more detail are:

- Pneumonia (ICD-9: 480-486)
- Emphysema (ICD-9: 492)
- Asthma (ICD-9: 493)
- Chronic Obstruction (ICD-9: 496) - Chronic Airways Obstruction NEC

Figure 2.48

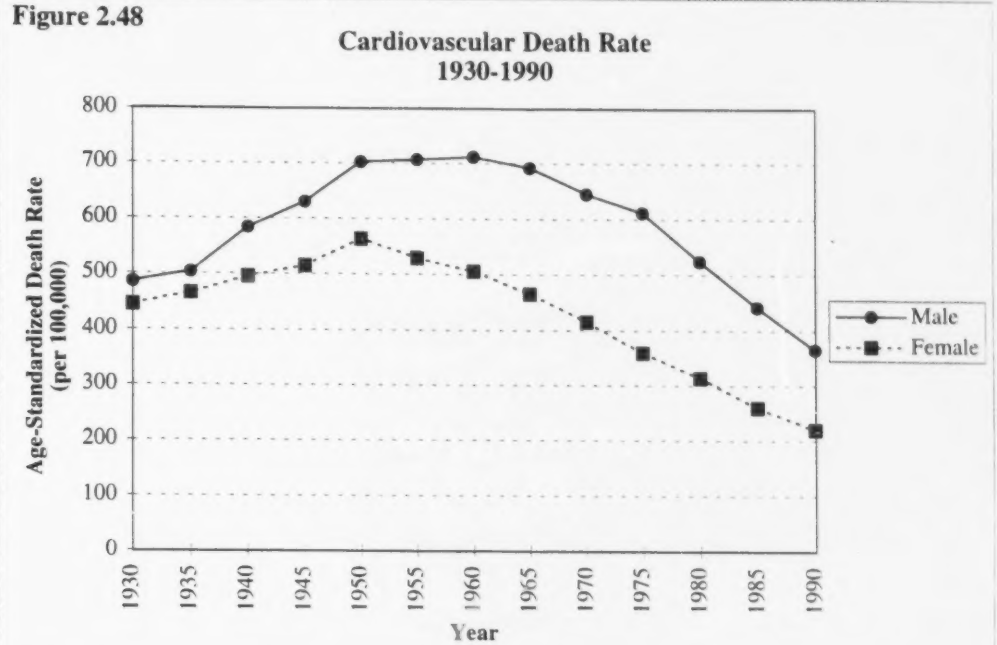
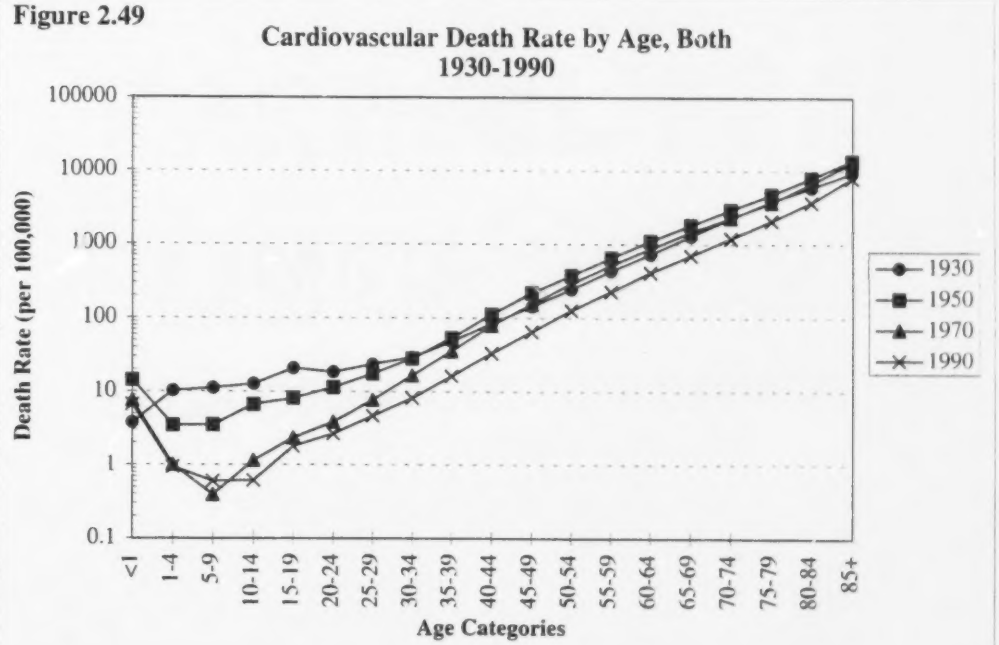


Figure 2.49



Data Source: see Table 2.4

Figure 2.50 Respiratory Deaths by Age, Males, 1993

Figure 2.51 Respiratory Death Rate by Age, Males, 1993

Figures 2.50 and 2.51 show the number of respiratory deaths by age and the respiratory death rate by age for males in 1993. Of the five major causes of death, respiratory deaths occur primarily in the older age groups. Significant numbers of deaths do not start occurring until the 60-64 age group.

Figure 2.52 Respiratory Deaths by Age, Females, 1993

Figure 2.53 Respiratory Death Rate by Age, Females, 1993

Figures 2.52 and 2.53 show the number of respiratory deaths by age and the respiratory death rate by age for females in 1993. Similarly for females, respiratory deaths occur primarily in the older age groups. However, for females, deaths from chronic airways obstruction are not as significant as in males.

2.9.3.6.2 Trend Evidence

Respiratory deaths are summarized for 1930 to 1990.

Figure 2.54 Respiratory Death Rate, 1930-1990

Figures 2.54 shows the respiratory death rate for males and females between 1930 and 1990. Respiratory deaths decreased sharply from 1930 to approximately 1950. For males they fluctuated but for females they continued to decrease. The changes in the classification system may have contributed to some of the fluctuations.

Figure 2.55 Respiratory Death Rate by Age, Both Sexes, 1930-1990

Figures 2.55 shows the respiratory death rate by age for males and females combined between 1930 and 1990. Most of the decrease in the death rates occurred for the younger age categories. For <1 there was an approximately 100 fold drop between 1930 and 1990.

2.9.3.7 External Causes

External causes cover a variety of different causes of death. A more suitable title that has been used is accidents and adverse effects. Accidents (or more appropriately fatal injuries) include motor vehicle accidents, falls, drownings, etc. The other important cause of death included in this category is suicide. In 1993, external causes were the cause of death for 8.5% of males and 4.5% of females.

Figure 2.50

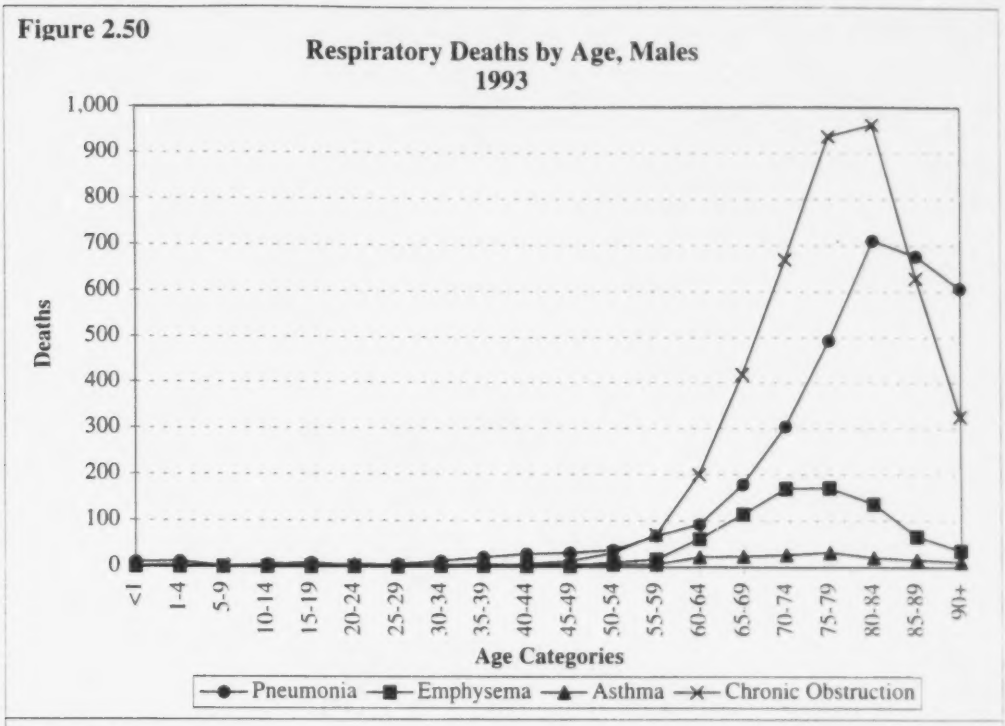
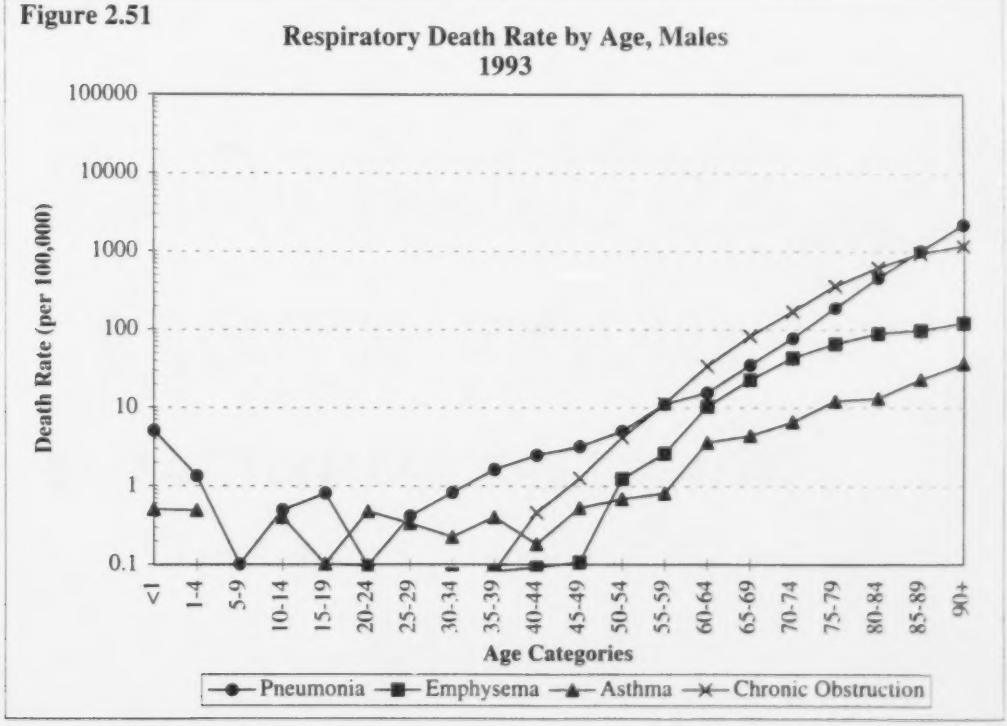


Figure 2.51



Data Source: Statistics Canada, 1995a

Figure 2.52

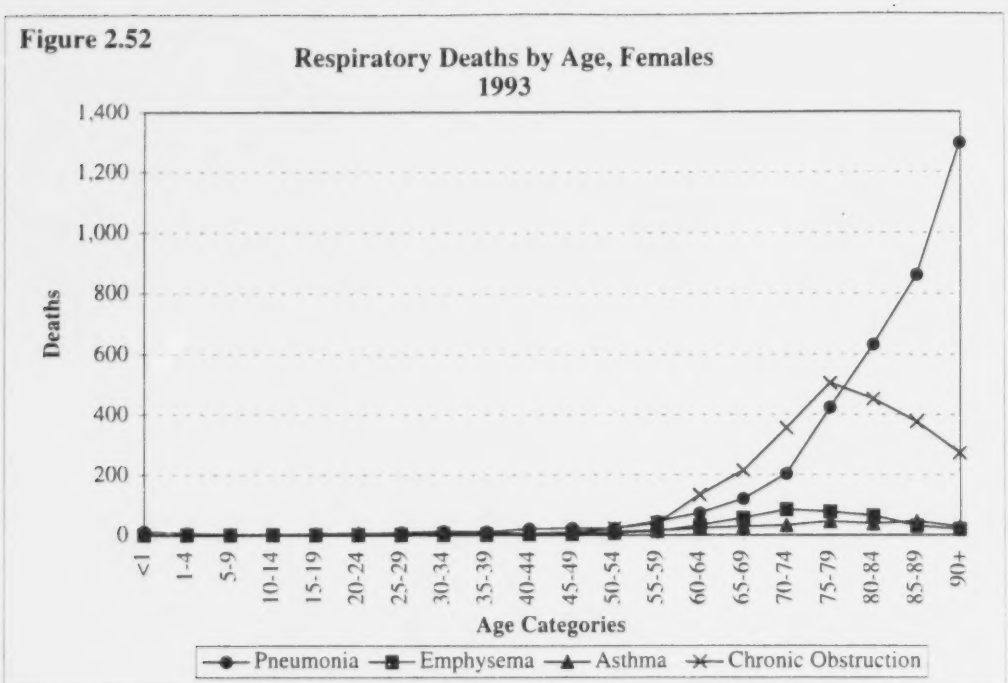
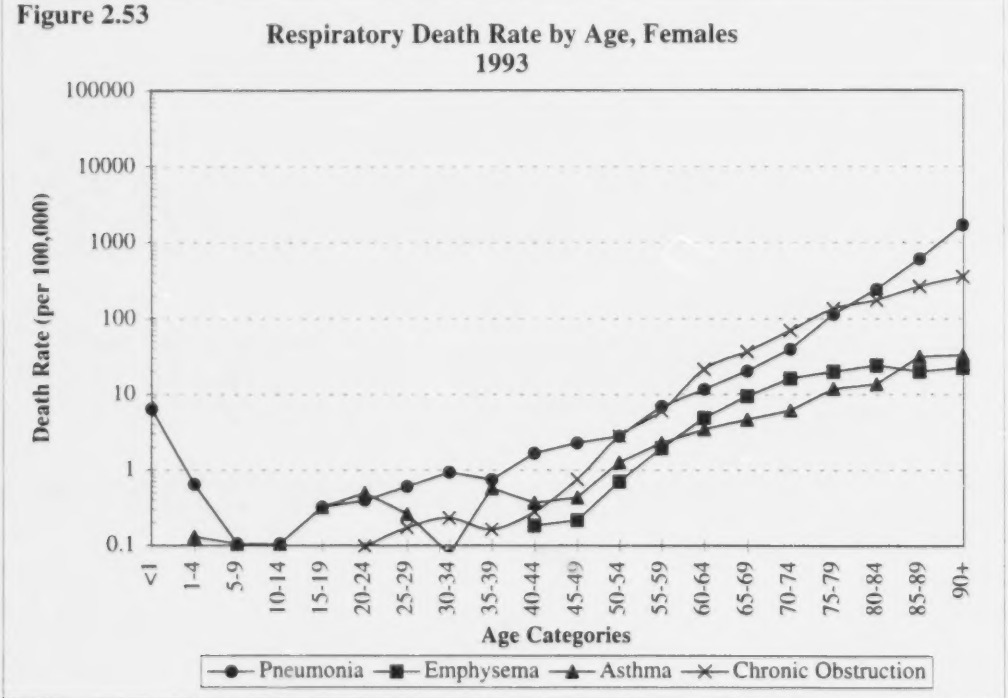


Figure 2.53



Data Source: Statistics Canada, 1995a

Figure 2.54

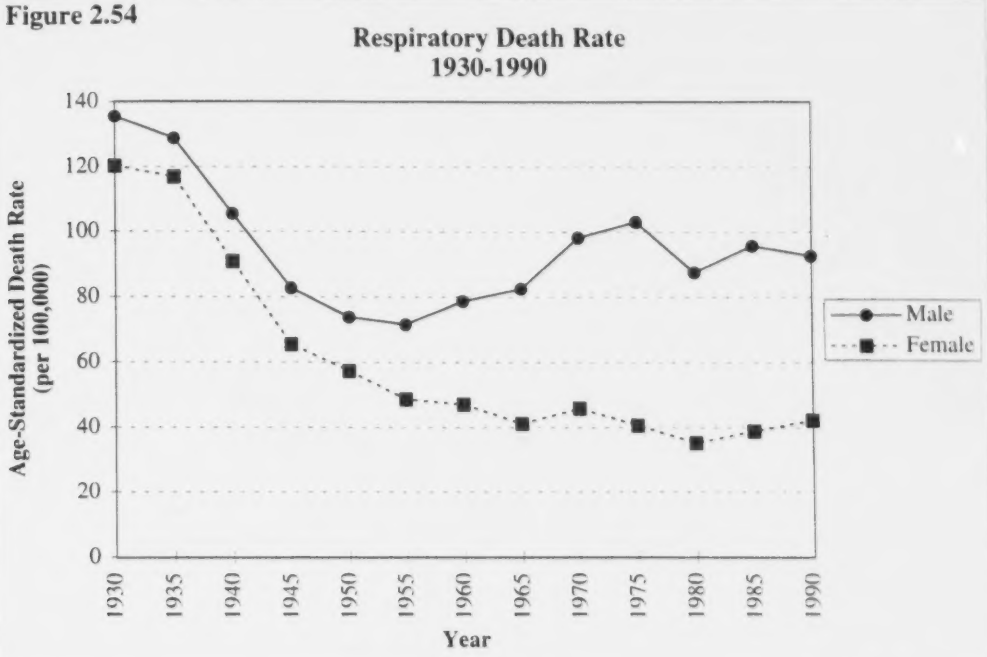
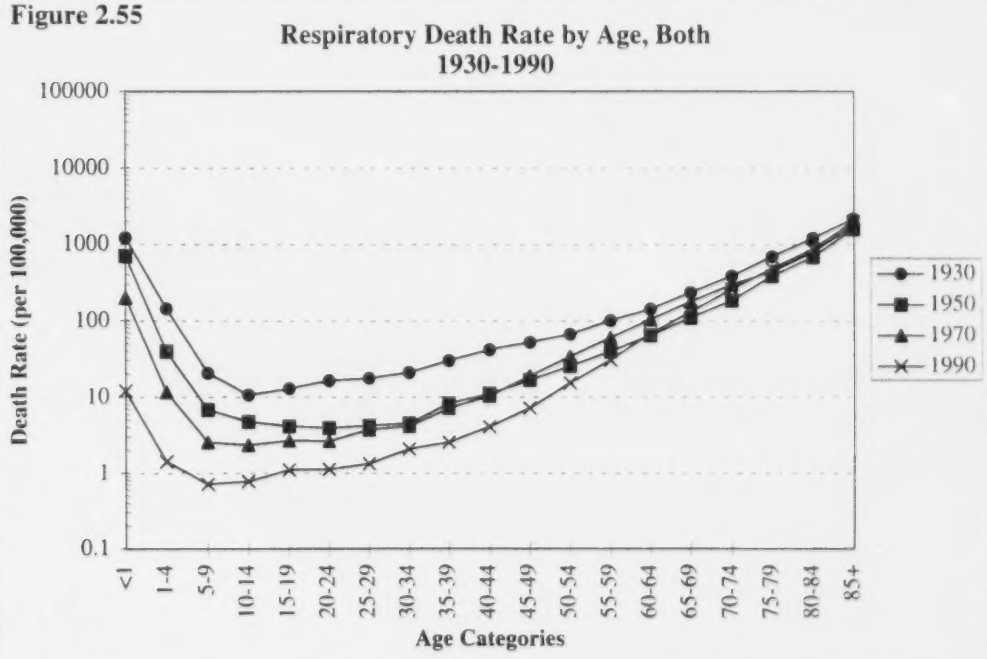


Figure 2.55



Data Source: see Table 2.4

2.9.3.7.1 1993 Evidence

External deaths separated by sex are summarized for the 1993.

The four sub-categories of external causes considered in more detail are:

- Auto Accidents (ICD-9: E810-E819) - Motor Vehicle Traffic Accidents
- Falls (ICD-9: E880-E888) - Accidental Falls
- Submersion/Suffocation (ICD-9: E910-E915) - Accidents, Submersion, Suffocation and Foreign Bodies
- Suicide (ICD-9: E950-E959)

Figure 2.56 External Deaths by Age, Males, 1993
Figure 2.56 External Death Rate by Age, Males, 1993
Figures 2.56 and 2.57 show the number of external deaths by age and the external death rate by age for males in 1993. Because of the diverse nature of sub-categories in external causes, large differences in the age distribution occur. Both motor vehicle accidents (auto traffic) and suicides are leading causes of death in male youth. Deaths from falls occur primarily in the elderly with an exponential increase in death rates beginning in those aged 60-64. Submersion or suffocation deaths were low and remained relatively constant (within 10 orders of magnitude) for all age categories.

Figure 2.58 External Deaths by Age, Females, 1993
Figure 2.59 External Death Rate by Age, Females, 1993
Figures 2.58 and 2.59 show the number of external deaths by age and the external death rate by age for females in 1993. For females, motor vehicle accidents and suicides are significantly lower than males. Deaths from falls is highlighted in these figures. The annual death rate from falls is less than 1 per 100,000 before the 50-54 age category and is 100 per 100,000 by the 80-84 category and continues to rise exponentially.

2.9.3.7.2 Trend Evidence

External deaths are summarized for 1930 to 1990.

Figure 2.56

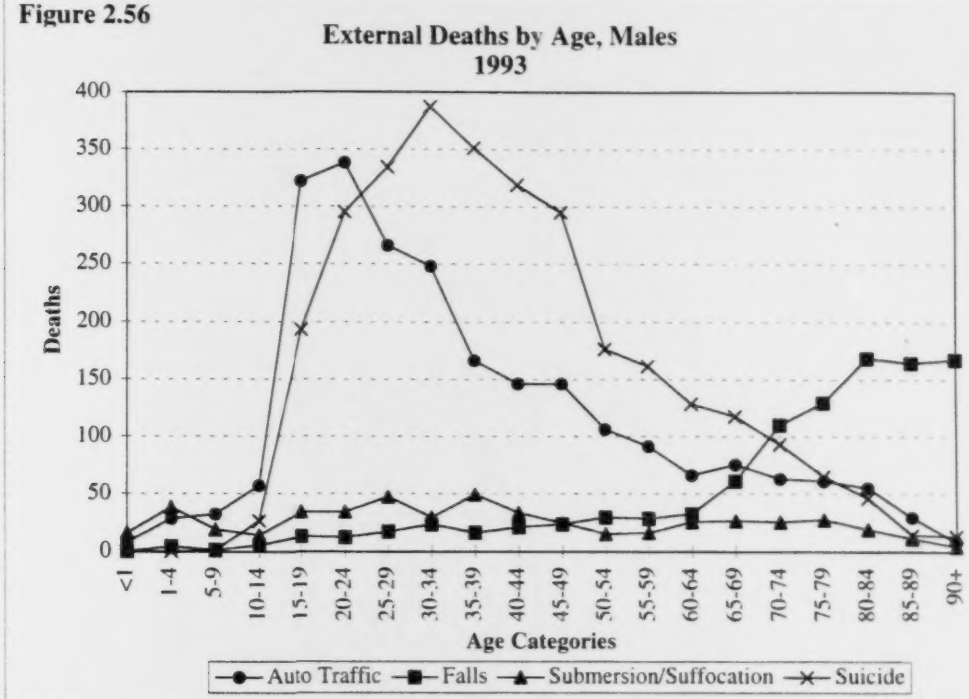
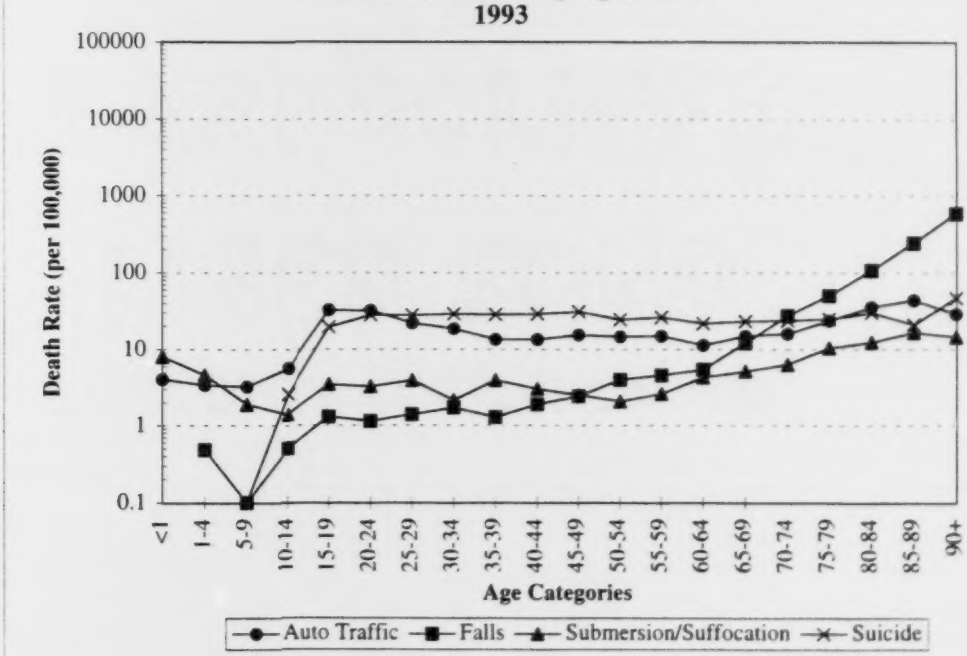


Figure 2.57



Data Source: Statistics Canada. 1995a

Figure 2.58

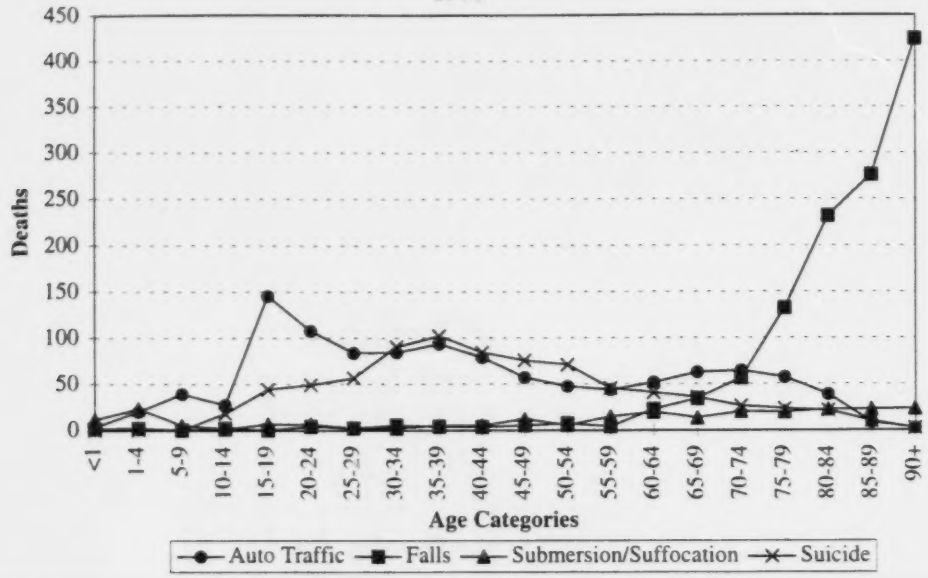
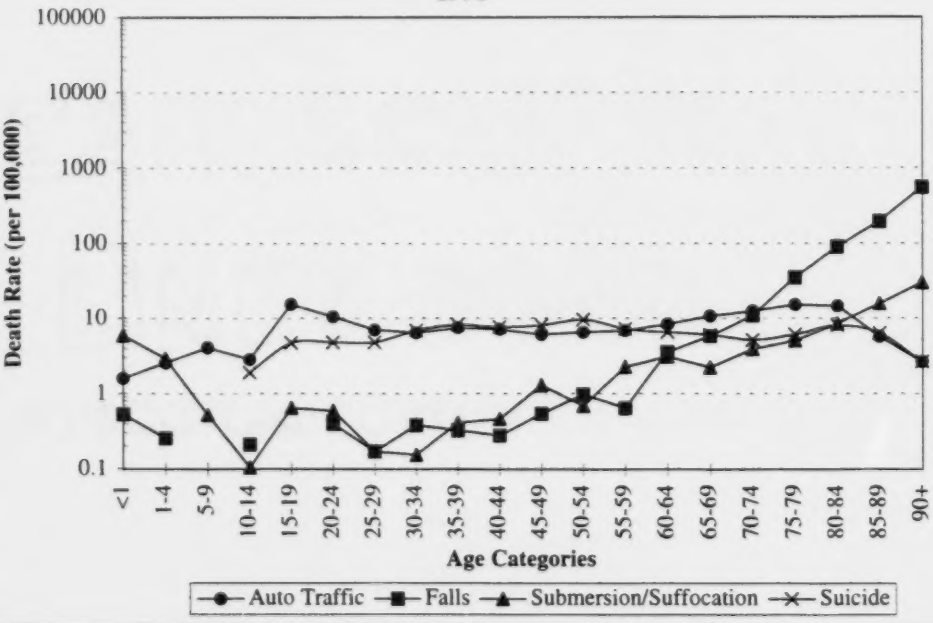


Figure 2.59



Data Source: Statistics Canada, 1995a

Figure 2.60 External Death Rate, 1930-1990

Figure 2.60 shows the external death rate for males and females between 1930 and 1990. External death rates have remained relatively constant until approximately 1975 when a decrease, more significant in males, began. This figure shows the substantial differences in the external death rate between males and females. Females have consistently had a death rate from external causes 2 to 3 times lower than males.

Figure 2.61 External Death Rate by Age, Both, 1930-1990

Figure 2.61 shows the external death rate by age for males and females combined between 1930 and 1990. As mentioned for Figure 2.60 the death rate for external causes has remained relatively constant. The decrease in deaths between 1970 and 1990 have occurred at the younger ages (<1 to 10-14) and middle (45-49 to 65-69) ages.

2.9.4 Maternal Deaths

Maternal deaths are defined as deaths to a mother due to complication during pregnancy, childbirth, or the pueperium (Statistics Canada, 1995a).

2.9.4.1 1993 Evidence

In 1993 there were 15 maternal deaths. By comparison there were over 388 thousand live births.

2.9.4.2 Trend Evidence

Maternal deaths are summarized for 1930 to 1990.

Figure 2.62 Total Maternal Deaths, 1930-1990

Figure 2.63 Maternal Death Rate, 1930-1990

Figures 2.62 and 2.63 shows the maternal deaths and maternal death rate between 1930 and 1990. Of all changes in mortality between 1930 and 1990, maternal mortality has been one of the most significant. Between 1930 and 1990 the number of maternal deaths dropped from over 1,400 to consistently less than 20. When expressed as a rate the drop has been even more significant, over 100 fold, since more births are occurring presently compared to the past. The drop in maternal deaths has similarities to infant deaths (Figure 2.13).

Figure 2.60

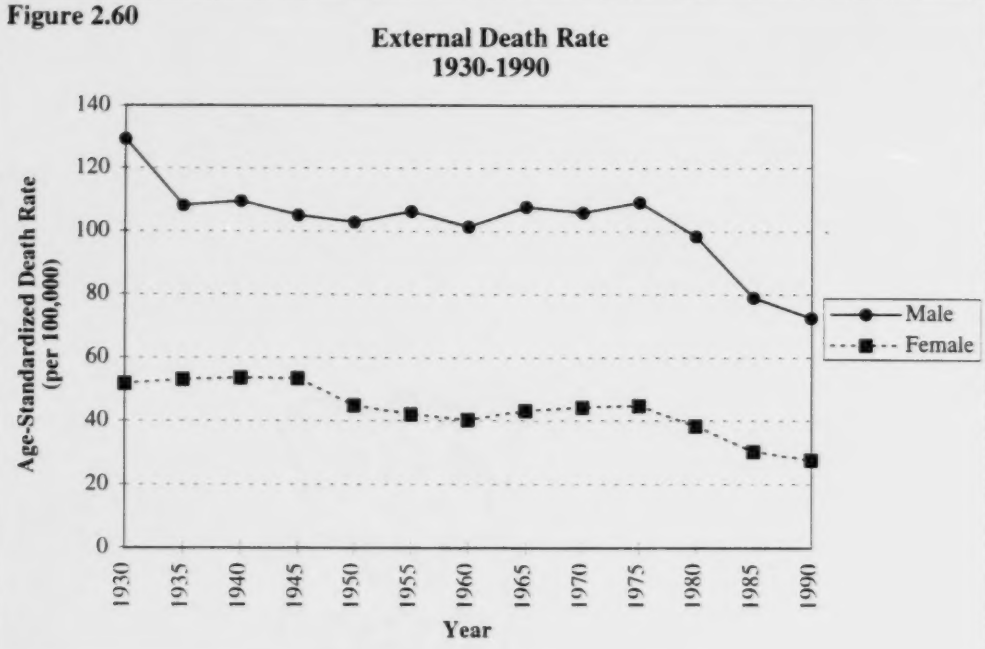
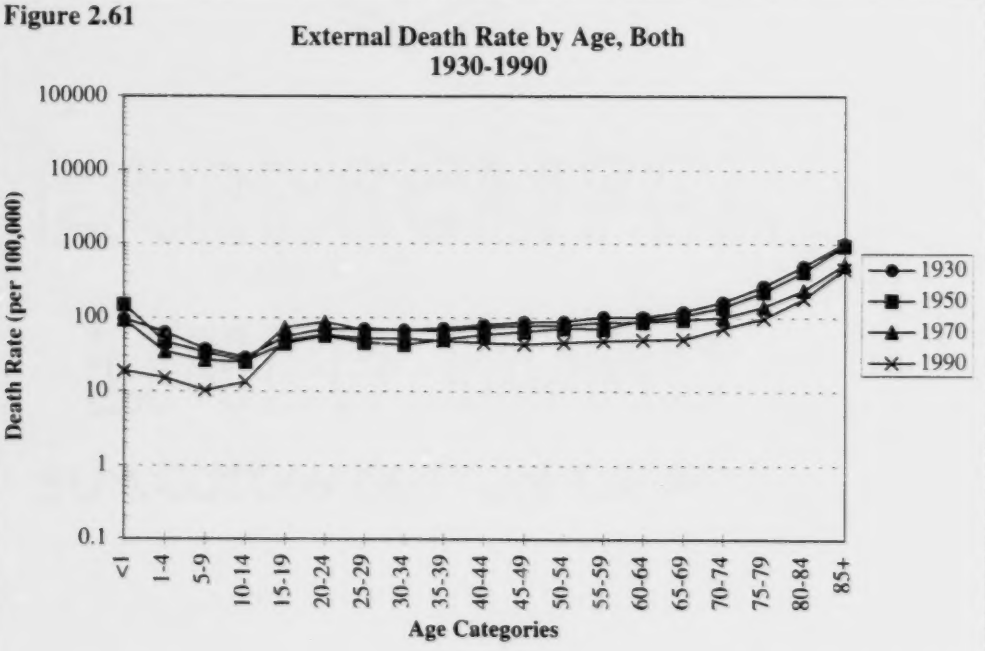


Figure 2.61



Data Source: see Table 2.4

Figure 2.62

Total Maternal Deaths
1930-1990

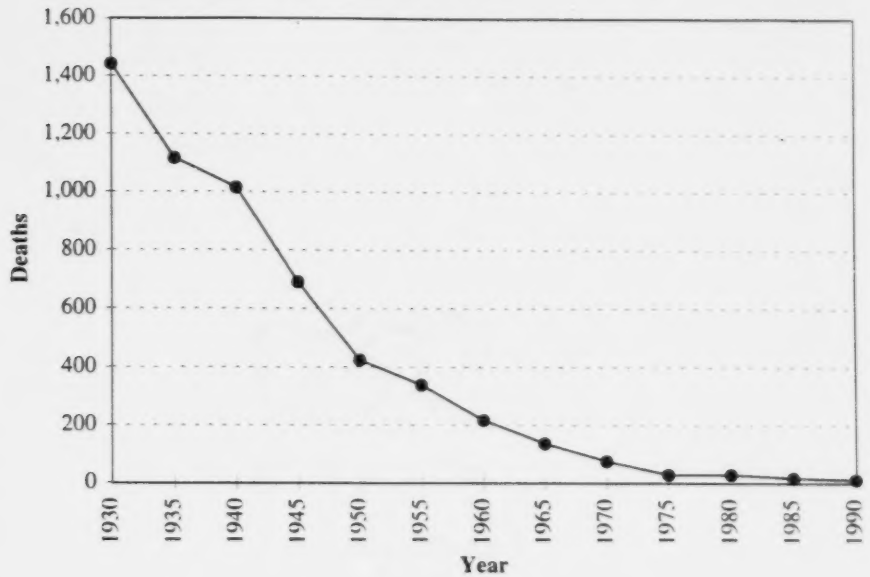
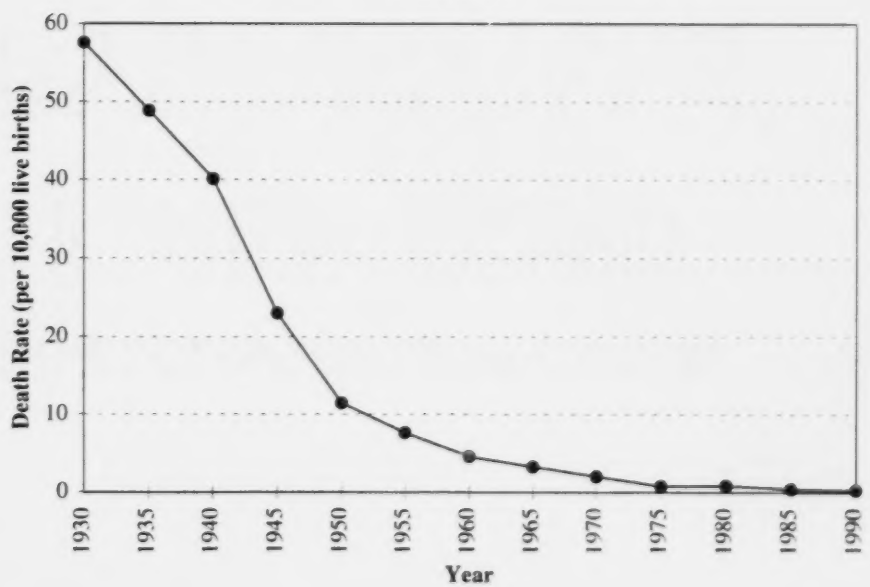


Figure 2.63

Maternal Death Rate
1930-1990



Data Source: Statistics Canada, 1994c

2.9.5 Potential Years of Life Lost

Death of younger people are a concern because these deaths are often more preventable and there is a greater sense of loss when someone has not lived their full potential life. For this reason, instead of only relying on total death counts and various death rates another method for accounting for mortality is potential years of life lost (PYLL). PYLL is a method used to compare different causes of death which gives more weight to deaths at younger ages.

As an example, you may decide to only be concerned with deaths before aged 75, what might reasonably be considered premature deaths. If a 12 years old dies then there would be 63 years (75-12) of life lost for that individual. The older the age of the individual at death, the fewer years of loss would be calculated until 75, at which point they no longer contribute to the calculation. When this calculation is done for specific causes of death, it effectively weights deaths based on the age at death.

One source of confusion with PYLL is that there are a variety of methods for doing the calculations. Because normally cause specific information is divided into 5 year age categories, all methods use the midpoint as the age at death. For example, all deaths in the 10-14 age category are assumed to be deaths at 12.

The first difference between methods for PYLL is the age that will be used as a reference. The choices include:

1. selecting a single reference age for both males and females (e.g. 75)
2. selecting different references ages for males and females, often the average life expectancy (e.g. males - 75, females - 81)
3. selecting the expected years of life remaining for males and females in <u>each</u> age category with no age reference

A second difference is whether to use:

1. the total number of deaths for each age category
2. the deaths rates for each age category

The Canadian Cancer Statistics (1996) used the expected years of life remaining in each age category with the total number of death in each category. Others have used a single age

reference with age-standardized death rates which allows comparison of PYLL values from different years (Wilkins et al., 1992).

This section does not attempt to review which method is preferred for calculating the PYLL. Each method weights the information differently and will yield slightly different results which are not directly comparable. However, all methods will give results which emphasize causes that kill the young and will de-emphasize causes that kill at older ages.

For my calculations I have selected the simplest method for calculating PYLL, using the same reference age for both males and females and using the total number of deaths for each age category.

2.9.5.1 1993 Evidence

To compare PYLL results with those from other types of direct evidence, I decided to compare the total number of deaths in 1993 with PYLL. Because the generated values are not comparable, the percentage of the total for each method for the 17 major categories was calculated. In addition, three different age cutoffs were used to see what effect this has on the results. These results are shown in Table 2.16 for males and Table 2.17 for females with the five major causes of death highlighted.

Table 2.16 Percentage of Total Deaths vs. PYLL, Males, 1993

Table 2.17 Percentage of Total Deaths vs. PYLL, Females, 1993

As expected, the PYLL placed considerably more weight on causes which killed the young. For males, the PYLL at 75 years places external causes, which resulted in 8.5% of deaths as the leading cause of PYLL. Cancer remained in second place while cardiovascular disease dropped to third. At the extremes were perinatal conditions and respiratory diseases. There were over 17 times as many deaths from respiratory diseases than perinatal conditions, but the PYLL ranked perinatal ahead because the respiratory deaths occurred primarily in the aged.

For females, cancer was the number one ranked PYLL followed by cardiovascular diseases and then external causes. For cancer PYLL shows how overall the effects of cancer influence female mortality at younger ages than male mortality. The PYLL increased the percentage allotted to cancer in females but decreased the same for males.

Table 2.16 Percentage of Total Deaths vs. PYLL, Males, 1993

No.	Shortened Name	% of Total Deaths	% of PYLL		
			@65 yrs	@75 yrs	@85 yrs
I	Infectious Diseases	**2.1**	**6.8**	**5.5**	**4.3**
II	Cancer	**28.3**	**16.2**	**22.5**	**26.1**
III	Endocrine and Others	2.7	1.8	2.1	2.3
IV	Blood Diseases	0.3	0.3	0.2	0.3
V	Mental Disorders	1.6	1.1	1.1	1.2
VI	Nervous System Diseases	2.4	2.5	2.2	2.2
VII	Cardiovascular Diseases	**37.0**	**14.0**	**20.5**	**26.1**
VIII	Respiratory Diseases	**9.1**	**2.2**	**3.2**	**4.7**
IX	Digestive Diseases	3.6	2.9	3.4	3.5
X	Genito-Urinary Diseases	1.5	0.5	0.6	0.8
XI	Pregnancy Related	-	-	-	-
XII	Skin Diseases	0.1	<0.1	<0.1	<0.1
XIII	Musculo-Skeletal Diseases	0.2	0.1	0.1	0.1
XIV	Congenital Anomalies	0.6	5.1	3.4	2.3
XV	Perinatal Conditions	0.6	6.3	4.1	2.7
XVI	Ill-Defined	1.5	4.6	3.6	2.8
E XVII	External Causes	**8.5**	**35.6**	**27.3**	**20.4**

Data Source: Statistics Canada, 1995a

Table 2.17 Percentage of Total Deaths vs. PYLL, Females, 1993

No.	Shortened Name	% of Total Deaths	% of PYLL		
			@65 yrs	@75 yrs	@85 yrs
I	Infectious Diseases	**0.9**	**2.2**	**1.8**	**1.5**
II	Cancer	**27.4**	**30.8**	**36.8**	**37.4**
III	Endocrine and Others	3.6	2.4	2.8	3.2
IV	Blood Diseases	0.5	0.4	0.4	0.4
V	Mental Disorders	2.3	0.8	0.8	1.0
VI	Nervous System Diseases	3.3	3.3	3.0	3.0
VII	Cardiovascular Diseases	**40.2**	**9.6**	**15.2**	**22.4**
VIII	Respiratory Diseases	**8.5**	**3.3**	**4.1**	**5.2**
IX	Digestive Diseases	3.8	2.6	3.1	3.4
X	Genito-Urinary Diseases	1.7	0.6	0.8	1.1
XI	Pregnancy Related	<0.1	0.2	0.1	0.1
XII	Skin Diseases	0.1	0.1	0.1	0.1
XIII	Musculo-Skeletal Diseases	0.6	0.6	0.6	0.6
XIV	Congenital Anomalies	0.5	7.9	5.1	3.2
XV	Perinatal Conditions	0.5	8.5	5.4	3.3
XVI	Ill-Defined	1.6	5.2	3.8	2.8
E XVII	External Causes	**4.5**	**21.8**	**16.3**	**11.6**

Data Source: Statistics Canada, 1995a

The information on PYLL shown in Tables 2.16 and 2.17 can be manipulated depending on the age cutoff that is selected. People concerned with external causes can select a lower age cutoff to emphasize this category while people concerned with cancer or cardiovascular diseases can select a higher age cutoff to emphasize these categories.

One important point to remember when PYLL is calculated using an age cutoff is that you are only using a percentage of all deaths in your calculations. The lower the age cutoff the lower the percentage of all deaths being used in the calculations. Table 2.18 shows the percentage of all deaths included for the three different age cutoffs. Because males have a higher mortality at any given age than females, a greater percentage have died by each age cutoff. With a 75 yr age cutoff, 56% of the male population was included versus 38% of the females population.

Table 2.18 Percentage of Population Included Using 65, 75 and 85 Year Age Cutoffs

When only looking at one gender, percentages are much easier to use than PYLL values. However when comparing genders, the PYLL values are useful because they take into account the number of people dying. Table 2.19 shows the sum of PYLL values for all causes using three different cutoff years. Males have a substantial greater total number of PYLL than females. This is related to the percentages in Table 2.18.

Table 2.19 Comparison of Male and Female Total PYLL, 1993

PYLL is a method highlighting that causes of death have different impacts for different age categories. By placing more weight on younger deaths PYLL emphasizes those causes of deaths that deprive individuals of life into old age.

2.9.6 Loss of Life Expectancy

Loss of life expectancy (LLE) is another way to incorporate the age at death into calculations. An advantage of loss of life expectancy, is that the result is a number which an individual may understand in personal terms.

The concept behind LLE is fairly straightforward. The basis for the calculations are the deaths rates by age categories (see Figure 2.7) [other methods can be used to calculate LLE information by age category is not available, (Cohen, 1991)]. The death rate in the first year of life is high, followed by a sharp drop and then an exponentially rising rate starting

Table 2.18 Percentage of Population Included Using 65, 75 and 85 Year Age Cutoffs

Gender	PYLL		
	@65 yrs	@75 yrs	@85 yrs
Male	30.5%	55.9%	84.6%
Female	19.1%	38.2%	68.6%

Data Source: Statistics Canada, 1995a

Table 2.19 Comparison of Male and Female Total PYLL, 1993

Gender	PYLL		
	@65 yrs	@75 yrs	@85 yrs
Male	628,409	1,107,613	1,894,671
Female	335,134	610,233	1,128,939

Data Source: Statistics Canada, 1995a

in the teens. This same population has a fixed calculated life expectancy for 1993. What LLE does is to take a cause, say cancer, which has a death rate of its own, and subtract it from total death rate for the year. It is as if a cure were found and people only die from the remaining causes, now at a lower rate. By reducing this rate, the life expectancy increases. The difference between the new life expectancy (without cancer mortality) and the actual life expectancy with (cancer mortality) is the LLE.

The greater the reduction in death rate from a cause, the larger will be its impact. Age is an important factor since reducing the death rate earlier in life will cause a larger improvement in overall life expectancy.

Table 2.20 shows the life table that was used to calculate the LLE for males, a similar table was used for females. There is no need to describe how the life table works in detail. For purposes of explaining LLE there are only two areas of importance. The first is the fifth column over, labeled q_x. This column is the annual mortality rate for that age category, the data from Figure 2.7. It is used to calculate all the values in the rest of table. The second important number in the first one in last column e_x which is the life expectancy. The difference between this number, and the new number after the mortality rates have been changed to reflect the absence of the disease is the LLE.

Table 2.20 Life Table, Males, 1993

Several simplifications were made in calculating these values. The first is with the life table. Ideally you want to use a life table separated into individual years. Unfortunately the only data on mortality was divided into the age categories used in previous sections. Therefore these mortality values were used to calculate the life table. Because the ages were limited by the 90+ cutoff and were in age categories, the estimated life expectancy was several years lower than the actual life expectancy. The errors this will cause in the final results is unknown, but because the important value is the difference between life expectancy, the errors should be minimized.

2.9.6.1 1993 Evidence

Tables 2.21 and 2.22 summarize LLE calculations for males and females in 1993.

Table 2.20 Life Table, Males, 1993

	l_x	d_x	p_x	q_x	L_x	T_x	e_x
<1	100,000	690	0.99310	0.00690	99,655	7,358,533	73.59
1-4	99,310	147	0.99852	0.00148	396,944	7,258,878	73.09
5-9	99,163	85	0.99915	0.00085	495,601	6,861,934	69.20
10-14	99,078	108	0.99891	0.00109	495,120	6,366,333	64.26
15-19	98,970	418	0.99578	0.00422	493,805	5,871,212	59.32
20-24	98,552	504	0.99489	0.00511	491,501	5,377,407	54.56
25-29	98,048	556	0.99433	0.00567	488,852	4,885,907	49.83
30-34	97,493	669	0.99313	0.00687	485,789	4,397,055	45.10
35-39	96,823	861	0.99111	0.00889	481,963	3,911,266	40.40
40-44	95,962	1,085	0.98869	0.01131	477,097	3,429,303	35.74
45-49	94,877	1,572	0.98343	0.01657	470,455	2,952,205	31.12
50-54	93,305	2,469	0.97354	0.02646	460,353	2,481,750	26.60
55-59	90,836	4,098	0.95488	0.04512	443,935	2,021,397	22.25
60-64	86,738	6,371	0.92655	0.07345	417,762	1,577,462	18.19
65-69	80,367	9,770	0.87843	0.12157	377,409	1,159,700	14.43
70-74	70,597	13,579	0.80765	0.19235	319,036	782,291	11.08
75-79	57,017	17,593	0.69144	0.30856	241,104	463,255	8.12
80-84	39,424	19,259	0.51150	0.48850	148,974	222,151	5.63
85-89	20,165	15,613	0.22577	0.77423	61,795	73,177	3.63
90+	4,553	4,553	0.00000	1.00000	11,382	11,382	2.50

Data Source: Statistics Canada, 1995a

Table 2.21 Total Deaths and LLE, Males, 1993
Table 2.22 Total Deaths and LLE, Females, 1993

The modification in the percentage of total deaths by cause as a result of LLE calculations is fairly small. In the most extreme case, perinatal conditions, the relative percentage is increased by approximately a factor of three. None of the three leading causes of deaths changed rank using LLE. Although the percentage assigned to cancer remained similar for males, it increased almost 6% for females. This perspective highlights how cancer has a relatively greater impact at younger ages in females than in males.

What is really useful about LLE is how it provides a useful quantitative measure. For example, if infectious disease were eliminated in males, the increase in life expectancy would be 115 days. We must be careful not to misinterpret this value. Although the increase in life expectancy for the entire male population is 115 days, the increase in life specifically for those who actually die of an infectious disease would be much greater. The LLE is small because the number of deaths is small relative to the population.

What LLE illustrates is that even if a major cause of death is substantially reduced, the overall increase in life expectancy is moderated because most people die of something else. Therefore if cardiovascular disease was eliminated, people would die more often from other causes.

Table 2.21 Total Deaths and LLE, Males, 1993

No.	Shortened Name	% Total Deaths	LLE	
			%	Days
I	Infectious Diseases	**2.1**	**2.4**	**115**
II	Cancer	**28.3**	**28.2**	**1343**
III	Endocrine and Others	2.7	2.3	110
IV	Blood Diseases	0.3	0.3	13
V	Mental Disorders	1.6	1.2	58
VI	Nervous System Diseases	2.4	2.1	100
VII	Cardiovascular Diseases	**37.0**	**35.4**	**1690**
VIII	Respiratory Diseases	**9.1**	**6.8**	**323**
IX	Digestive Diseases	3.6	3.2	152
X	Genito-Urinary Diseases	1.5	1.0	49
XI	Pregnancy Related	-	-	-
XII	Skin Diseases	0.1	<0.1	2
XIII	Musculo-Skeletal Diseases	0.2	0.2	7
XIV	Congenital Anomalies	0.6	1.4	69
XV	Perinatal Conditions	0.6	1.7	83
XVI	Ill-Defined	1.5	1.9	90
E XVII	External Causes	**8.5**	**11.9**	**565**

Data Source: Statistics Canada, 1995a

Table 2.22 Total Deaths and LLE, Females, 1993

No.	Shortened Name	% Total Deaths	LLE	
			%	Days
I	Infectious Diseases	**0.9**	**1.1**	**40**
II	Cancer	**27.4**	**33.2**	**1251**
III	Endocrine and Others	3.6	3.3	124
IV	Blood Diseases	0.5	0.4	15
V	Mental Disorders	2.3	1.4	52
VI	Nervous System Diseases	3.3	3.0	113
VII	Cardiovascular Diseases	**40.2**	**33.9**	**1281**
VIII	Respiratory Diseases	**8.5**	**6.5**	**245**
IX	Digestive Diseases	3.8	3.4	127
X	Genito-Urinary Diseases	1.7	1.3	50
XI	Pregnancy Related	<0.1	<0.1	1
XII	Skin Diseases	0.1	0.1	3
XIII	Musculo-Skeletal Diseases	0.6	0.6	21
XIV	Congenital Anomalies	0.5	1.8	66
XV	Perinatal Conditions	0.5	1.8	68
XVI	Ill-Defined	1.6	1.8	69
E XVII	External Causes	**4.5**	**6.6**	**247**

Data Source: Statistics Canada, 1995a

2.10 Uncertainty

Overall health risk estimates based on direct evidence have low uncertainty. Unlike other sources of evidence, direct evidence is based on a fixed outcome and individual evidence is supplied by an informant or filled in by the medical establishment.

Several sources of uncertainty can affect mortality data:

> "trends in mortality data may be artifactual, reflecting changes in coding practices (e.g., ICD revisions, training of physicians), diagnostic capabilities (e.g. new tests, procedures for assigning diagnoses), and the denominator population (changing geographic coverage or census inaccuracies)." (Lilienfeld et al., 1994, pg.72)

Lilienfeld and Stolley (1994) summarized some of the uncertainties that can be associated with mortality trends. These were divided into artifactual and real:

A. Artifactual

1. Errors in the numerator due to:
   - changes in the recognition of disease
   - changes in rules and procedures for classification of causes of death
   - changes in the classification code of causes of death
   - changes in accuracy of reporting age at death
2. Errors in the denominator due to errors in the enumeration of the population

B. Real

1. Changes in age distribution of the population
2. Changes in survivorship
3. Changes in incidence of disease resulting from:
   - genetic factors
   - environmental factors

In summary the estimated uncertainty for direct evidence is:

- total number of deaths - the most accurate piece of evidence. The uncertainty is less than 0.1%. Once the total is used to calculate population-based rates the uncertainty is caused by the population estimates. Rates should have an uncertainty less than 5%

- deaths by age and sex - dividing the total number of deaths by age and sex should only have a minor increase in the uncertainty, less than 0.1% overall. Once expressed as a rate the uncertainty should be less than 5%. However, age-specific rates will have greater uncertainty but they should be less than 10%.
- cause of death - the uncertainty by major categories will vary between categories but should range from less than 1% to under 5%. The uncertainty by three digit ICD code will also have tremendous fluctuations depending the cause of death, the age of the individual and any delays in reporting results. The majority should be less than 10% with a few 50% or greater.

3. INDIRECT EVIDENCE AND INFERENCE

Indirect evidence and inference is based on epidemiological studies. Epidemiology is used to evaluate risk factors influencing human health. This will be followed by a discussion of epidemiological risk factors. Risk factors have been separated into major individual risk factors and risk factors by major cause of death. This section concludes with a discussion of the uncertainties associated with indirect evidence and inference.

3.1 Epidemiology

Epidemiology can be defined as, "The study of the distribution and determinants of health-related states or events in specified populations, and the application of this study to control of health problems" Stedman's Medical Dictionary (1995). A more comprehensive definition which describes various aspects of epidemiologic study is:

> "The study of the distribution and determinants of health-related states in human and other animal populations. Epidemiological studies involve surveillance, observation, hypothesis-testing, and experiment. Distribution is established by analyzing the time, place, and class of person affected by a disease. Determinants may include physical, biological, social, cultural, and behavioral factors. Epidemiological methods are most commonly applied to the study of disease; however, they also may be used to examine causes of death (e.g., homicides of various sorts) or behaviors (e.g., tobacco or alcohol use, practice of safe sex, use of health services). Epidemiology plays a key role in formulation and implementation of public health policy." (Stedman's Medical Dictionary, 1995)

Analyzing the distribution of disease has a long history and is a foundation of epidemiology. However, identifying a determinant of a disease and applying it to the control of health problems can be traced back to London, England in the mid-nineteenth century. Dr. John Snow calculated the rates of cholera and he found large differences in the rates between populations served by different water companies. He thereby pioneered epidemiologic principles to propose that cholera was associated with the source of the water supply. Snow's analysis showed the basic logic for many subsequent studies which have been beneficial to the health of human populations. Most of the epidemiologic studies of the mid to late nineteenth and early twentieth centuries have addressed communicable diseases. More recently, epidemiology has expanded its scope to include a wide variety of other health problems including searching for risk factors associated with chronic diseases and accidents.

3.1.1 Measurement

The basic logic underlying an epidemiologic study is directed towards developing evidence of an association between a determinant of cause and a health outcome. This logic does not provide dichotomous yes or no answers. Rather it provides evidence along a continuum from weak to strong evidence of an association between a determinant or cause and an

effect or outcome. There are many types of measures for the strength of an association in epidemiology. However, only two are described and used in this section: relative risk and population attributable risk.

Table 3.1 shows the four basic categories where people can be placed in an epidemiological study with respect to exposure and disease. The rows indicate the exposure category. For example the exposure could represent smokers vs. nonsmokers, high alcohol consumption vs. low alcohol consumption, high vs. low education level, wearing vs. not wearing a seatbelt etc. Some categories may be discrete (seat belt or no seat belt) while others may be continuous (non-smokers, non-smokers with second-hand smoke, light smokers, heavy smokers). The columns indicate the disease (or outcome) that is being studied. For example this could represent the development of a specific cancer, mortality from cardiovascular disease, all cause mortality etc. Again, some categories may be discrete (death or no death) while others may involve a degree of impairment. For our purposes, we will simplify these complexities by dealing with these categories as if they are all discrete.

Table 3.1 Exposure vs. Disease

The relative risk or risk ratio (RR) is the ratio of the proportion of those with the disease (or outcome) who have been exposed, to the proportion of those with the disease who have not been exposed. Using the letters in Table 3.1 the relative risk is calculated with the following equation:

$$\frac{a/(a+b)}{c/(c+d)} = \frac{\text{disease (exposed) / total exposed}}{\text{disease (not exposed) / total not exposed}}$$

For any individual, relative risk provides an indication of how their risk of experiencing the disease might increase (as a multiplier) if they changed from unexposed to exposed, or conversely how much one could reduce risk (as a divisor) if one eliminated their exposure. Relative risk is usually accompanied by confidence intervals which indicate the statistical uncertainty of the value. The larger the confidence intervals (for the same specified confidence limit) the less certain one can be about the true value of the relative risk. Commonly, 95% confidence intervals have been used in epidemiological studies. Because a relative risk of 1.0 would arise if there was no association between the exposure and the disease, a study outcome is commonly regarded as statistically significant if the calculated confidence intervals do not include a relative risk of 1. However, these statistical confidence intervals do not account for non-statistical sources of uncertainty. This is

Table 3.1 Exposure vs. Disease

	Disease	No Disease
Exposure	a	b
No Exposure	c	d

discussed in more detail in the section on uncertainty at the end of this indirect evidence and inference section.

Many epidemiological studies only report the relative risk. From a public health perspective, we usually want to maximize the benefit to the largest number of people. For this reason, population attributable risk (PAR) is a more important public health measure than is relative risk. PAR uses the relative risk to estimate the excess risk across the entire study population. The higher the PAR, the larger the number of people affected by the factor. Therefore, a factor with a high relative risk but low proportion of the population exposed (e.g. breast cancer and the BRCA1 gene) can have a lower PAR than a factor with a low relative risk but high proportion of the population exposure (e.g. skin cancer and ozone) (Northridge, 1995).

3.1.2 Types of Epidemiological Study

There are several ways to classify and name the different types of epidemiological study. Table 3.2 provides a summary of several types of epidemiological study with alternative names and units of study. The most basic division is between observational and experimental studies, wherein the latter requires experimental intervention to control the exposures in the study along with a variety of other elements which are more actively controlled.

Table 3.2 Types of Epidemiological Study

The six types of epidemiological study identified in Table 3.2 are described in more detail.

1. Descriptive: often the first step in any epidemiologic investigation. Descriptive studies are usually based on death certificates and use historical information. No analysis of exposure versus effect is done. Example - examining age-standardized death rates for specific causes between countries.
2. Ecological: studies population rates and not individual responses, therefore no reliable associations with exposures can be made at the group level. The tendency of this design to yield spurious correlation is termed the ecological fallacy. This design is often used for studying rare diseases and is often used for hypothesis generation. Example - red wine consumption and heart disease.
3. Cross-sectional: measures exposure and effect at the same time to estimate the prevalence of disease. However, this design does not assure that exposure preceded disease which is necessary for supporting causal inferences. Good questionnaires and

Table 3.2 Types of Epidemiological Study

Type of Study	Alternative Name	Unit of Study
Observational studies		
1. Descriptive studies		
2. Ecological*	Correlational*	Populations
3. Cross-sectional	Prevalence	Individuals
4. Case-control	Case-reference	Individuals
5. Cohort	Follow-up	Individuals
6. Experimental studies		Patients, healthy people or communities

* although these names are widely used in epidemiological practice, neither is accurate in meaning for other scientific disciplines. Ecological studies have nothing to do with ecology and all epidemiological studies are fundamentally assessing the correlation factors, so all studies are correlational

Adapted from Beaglehole et al., 1993, Table 3.1

appropriate study population are needed to be sure exposure is representative of earlier periods. Example - random telephone survey of health habits

4. Case-control: include people with disease (or other outcome) and a control group which does not have the disease under study. Case-control studies are best for studying rare diseases, multiple exposures and determinants with long latent periods. These studies involve selecting the cases and the controls and then determining their status with regard to exposure. Example - thalidomide and birth defects
5. Cohort: begins with people free of disease who are then followed up over time either by reviewing past records (retrospective cohort) or following into the future (prospective cohort). A prospective cohort allows for more accurate measurement of exposure without the potential bias between cases and controls. This design provides much better information for inferring causation of disease and multiple outcomes. A major disadvantage is the long time required, the high cost, and the large size of cohort which must be followed for rarer types of disease to yield an adequate number of cases. Example - Framingham study of coronary heart disease
6. Experimental: several types including randomized controlled trials, field trials and community trials. Can be used to assess new preventive or therapeutic methods. The high degree of intervention inherent in experimental designs limits their use in risk factor epidemiology for ethical and practical reasons. Example - β-carotene cancer studies

Most of the epidemiological studies reported in this thesis are either case-control or cohort. However, the largest number of environmental epidemiology studies found in the literature are ecological or cross-sectioned studies (Saunders, 1996). The case control or cohort study designs can both provide quantitative estimates of health risks and can be used to study most risk factors.

3.1.3 Causal Inference

The types of epidemiological study can be arranged in a similar fashion to the uncertainty hierarchy shown in Figure 1.2. At the top of the hierarchy is descriptive, the weakest type of epidemiological study followed by ecological, cross-sectional, case-control, cohort and at the bottom the strongest type of epidemiological study, experimental. The stronger study designs are better at establishing associations or supporting causal inferences. On their own, epidemiological studies cannot establish causation, but better study designs can provide substantial evidence to support causal inferences.

Early epidemiological investigations focused on communicable diseases. Over 100 years ago the Henle-Koch postulates for infectious diseases were proposed. The Henle-Koch postulates are (Evans, 1976):

1. The parasite occurs in every case of the disease in question and under circumstances which can account for the pathological changes and clinical course of the disease.
2. It occurs in no other disease as a fortuitous and nonpathogenic parasite.
3. After being fully isolated from the body and repeatedly grown in pure culture, it can induce the disease anew.

Robert Koch concluded that if all three conditions could be satisfied, the "occurrence of the parasite in the disease can no longer be accidental, but in this case no other relation between it and the disease except that the parasite is the cause of the disease can be considered". Today infectious diseases are only one part of epidemiologic study and, as Koch noted, even many infectious diseases cannot meet the strict Henle-Koch postulates(Evans, 1976).

New rules have evolved to help determine the relative strength of associations in epidemiologic studies. Because associations could be the result of biases, confounders or random chance, additional evaluation is usually necessary to support causal inference. Hill prepared a famous set of nine guidelines to help in determining the strength of the associations for inferring causation (Hill, 1965). The WHO published a more recent list of eight guidelines for judging causation, several of which are the same as Hill's (Beaglehole et al., 1993):

1. Temporal relation - does the proposed cause precede the effect? This is especially challenging to satisfy for cancer because effects may not be recognized until ten or more years following initial exposure
2. Plausibility - is the association consistent with other knowledge of the biological mechanism of the disease?
3. Consistency - do several studies using a variety of designs in different settings show similar results?
4. Strength - how large and statistically significant is the relative risk?
5. Dose-response relationship - is there a consistent relationship between degrees of exposure to the cause (e.g. exposure to a chemical) and the proportion of individuals responding?
6. Reversibility - does removal of a possible cause reduce the rate of response?

7. Study design -recognizes the hierarchy of designs in their ability to generate evidence in support of causal inferences? (i.e. cohort studies can establish stronger causal associations than ecological studies)
8. Judging the evidence - because uncertainty always remains and risk factors rarely meet all the criteria, judgments must be made

3.2 Risk Factors

Epidemiology uses risk factors to detect individuals and populations at elevated risk and to determine causes. Risk factors in this thesis are defined as anything which is apparently or potentially related to increases or decreases in mortality or other health effects. This intentionally broad definition allows for risk factors that may not necessarily be the primary underlying causes of the effect.

Beaglehole et al. (1993) summarized four factors that play a part in the causation of a disease. These four factors provide a useful distinction for the different types of risk factors that will be explored in this section.

1. Predisposing factors: may create a state of susceptibility to a disease agent (e.g. age, sex, previous illness)
2. Enabling factors: may favor development of disease (e.g. low income, poor nutrition, bad housing, inadequate medical care)
3. Precipitating factors: exposure to a specific disease agent
4. Reinforcing factors: repeated exposure to the agent

There are two ways to summarize information on risk factors. The first is to look at individual risk factors and identify which causes of death (e.g. cancer or cardiovascular disease) it affects. The second is to start with a cause of death and identify the individual risk factors associated with it.

Individual risk factors are summarized in these four categories in Section 3.3. A comprehensive list of individual risk factors is shown in Table 3.3. Section 3.4 summarizes the individual risk factors as they relate to the five major causes of death from the direct information section.

Table 3.3 Individual Risk Factors Relating to Health

Table 3.3 Individual Risk Factors Relating to Health

1. Biological
- 1.1 Age
- 1.2 Sex
- 1.3 Genetics (Heredity)
- 1.4 Health

2. Lifestyle / Behavioral
- 2.1 Smoking
- 2.2 Alcohol
- 2.3 Drugs
- 2.4 Diet
- 2.5 Exercise
- 2.6 Weight
- 2.7 Sexual and Reproductive Factors
- 2.8 Safety
- 2.9 Personality
- 2.10 Stress

3. Societal
- 3.1 Education Level
- 3.2 Economic Status
- 3.3 Unemployment
- 3.4 Marital Status
- 3.5 Occupation
- 3.6 Geographic Area / Region
- 3.7 Medical
- 3.8 Transportation
- 3.9 Recreational
- 3.10 Other

4. Environmental
- 4.1 Air Pollution
- 4.2 Water Pollution
- 4.3 Food Additives and Contaminants
- 4.4 Chemicals
- 4.5 Radiation
- 4.6 Natural Disasters

3.3 Major Individual Risk Factors

Ideally, the approach of working from individual risk factors towards cause of death can be combined with reviewing causes of death in relation to associated individual risk factors. Moore (1985) was able to combine these two methods into a large table with a list of risk factors along the top and causes of death along the sides. This summary table is included in Appendix 3. Moore (1985) divided his list of risk factors into four categories based on Lalonde (1974): human biology, environment, lifestyle, health care. For this thesis, four similar categories were selected.

1. Biological - predisposing factors
2. Lifestyle / Behavioural - enabling, precipitating and reinforcing factors
3. Societal - enabling factors
4. Environmental - precipitating and reinforcing factors

Lalonde's fourth category, medical, was broadened and labeled societal. The usual type of risk factor (according to Beaglehole et al., 1993) is shown for each category as well.

Often, it is the combination of risk factors that greatly increases a person's risk, not only a single one (e.g. for cardiovascular disease - if the person is older, male, smokes, has high blood pressure and is a diabetic). However, many people who develop disease or have accidents have none of the known risk factors.

3.3.1 Biological

Biological risk factors are summarized in five subsections: age, sex, genetics, heredity and health. The two basic biological risk factors are an individual's age and sex. These are predisposing risk factors, ones that cannot be changed. Information was previously presented in the direct information section on age and sex relating to mortality. Two additional biological risk factors that are predisposing are genetics and heredity. The final risk factor in the biological section is a general one, health, which describes the health risk associated with blood pressure, cholesterol and diabetes.

3.3.1.1 Age

Age is one of the strongest risk factors related to health. Though a complete range of health status occurs at all age levels (e.g. healthy people through to those dying and deceased), on average there is a consistent and exponential increase in mortality and other health effects starting in the teens. This trend was shown in the direct evidence section (see Figure 2.8).

But, the overall mortality rate is not the only concern, the percentage of death from specific causes is important as well. Even though the mortality rate for accidents is higher at older ages (85+), they are not the leading causes of death in that age range while accidents are leading causes of death in young adults. A similar relationship between age and different causes of death occurs for individual risk factors.

Age is such a strong risk because aging is a natural process. As the body ages, individual organs and systems accumulate damage over time so the body weakens and becomes more susceptible to injury and disease.

3.3.1.2 Sex

Although the sex of an individual is not as strongly related to mortality as age, it is still an important and consistent risk factor. There are two basic differences in risk factors associated with sex, they can be grouped into the anatomical and non-anatomical risk factors.

Anatomical differences occur for reproductive system-related causes of death. Men may die of the prostate cancer while women may die of breast and ovarian cancer. In addition, hormonal differences have been linked with mortality because before menopause, female hormones help protect women against cardiovascular disease. As an aside, men also die of breast cancer, but at a rate over 100 times lower than women. In the case of breast cancer, hormonal differences may explain the large differences between men and women for cancer at an anatomical site which occurs in both sexes.

Non-anatomical differences help explain the increased mortality in men for most causes of death. Some these differences are associated with lifestyle/behavioural and societal risk factors in addition to biology.

3.3.1.3 Genetics (Heredity)

We must distinguish between heredity and genetics. Heredity is the transmission of characteristic traits and qualities from parents to their children, in the form of genetic characteristics which are correctly transcribed in the offspring. Congenital defects, one of the leading causes of death in infants are mostly genetic but are not necessarily related to hereditary, in that they can arise from errors in genetic transcription from the parent to the offspring.

For cardiovascular disease, genetics play an important role in the development and contribute to the susceptibility or resistance to the disease (WHO, 1994).

> "the risk of heart disease in a given individual or community reflects the interplay between genetic susceptibility to disease and environmental factors such as diet, physical exercise, ambient temperature, and smoking habits" (Swales et al., 1993, pg. 12)

Genetics plays a role in many forms of cancers. Most of the common genetic markers that have been identified have a low relative risk, but some more rare factors have high relative risks. The National Research Council (1994) in the U.S. identified several factors related to genetics which may affect the cancer susceptibility: carcinogen metabolism, DNA-Adduct formation, DNA- repair rates. DNA adducts are sites on the genetic code which become damaged by the attachment of a reactive chemical compound. These adducts can give rise to subsequent errors in the replication of DNA when cells divide or in the reading of the genetic code for guiding cellular metabolism. They noted that:

1. variations of several thousand have been observed for some metabolic activities.
2. interindividual variation and intertissue variation for formation of DNA adducts range by a factor of 10-150 among humans.
3. five fold variation have been observed in DNA repair rates.

A recent advance that has been gaining momentum and interest is identifying genes that are associated with increased risk for various diseases (notably cancer). People who have these gene sequences can have relative risks which are orders of magnitude greater than those without. Most of the discoveries to date have been for gene sequences that are less common in the general population. However, in the future, this research could help identify individuals with higher susceptibilities to common cancers and this could lead to improved preventive practices. This genetic research raises important ethical issues relating to genetic testing of fetuses, and identification and patient notification of incurable diseases.

Heredity is closely linked with genetics, being the transmission of genetically determined characteristics from parents to children. Examples include physical characteristics like eye colour and blood type.

For cancer, heredity appears to contribute particularly to childhood and early adulthood cancers but likely affects the susceptibility to all cancers (Ames et al., 1995). A very

specific example of this is retinoblastoma, cancer of the eye, which is typically found in young children. Parents with susceptible genes have a 50% chance of passing it on to their offspring.

3.3.1.4 Health

This category highlights some of the risk associated with blood pressure, cholesterol levels and diabetes. In addition to these, the general state of health is closely linked with other health effects. Poor health can increase the susceptibility of the body which can allow other diseases or ill effects to occur. An extreme example of this is AIDS which weakens the immune system allowing otherwise innocuous diseases to ravage the body.

Blood pressure is a measure of hypertension, which was identified as a health risk with the help of the insurance industry in the U.S. in the late 1950s (Society of Actuaries, 1980) High blood pressure can lead to heart attack, stroke, blindness, kidney failure and can double the risk of heart disease. High blood pressure can be present without symptoms and unfortunately researchers do not know the cause of the majority of cases. Overall, age-adjusted risk of stroke among hypertensives (with high blood pressure) compared to normotensives (with normal blood pressure) is 3.1 for men and 2.9 for women. There is good clinical evidence that treating isolated systolic hypertension in those over 60 years of age will decrease the incidence of cardiovascular disease (Heart and Stroke Foundation of Canada, 1995).

Cholesterol is mostly produced by our livers and only 1/3 comes from the food we eat. Diet, heredity, smoking and weight influence our cholesterol level. The type of cholesterol and fat is important as well. Serum cholesterol levels increase with higher intake of saturated fats, decrease with higher intake of polyunsaturated fats and are not changed by monounsaturated fats. Higher levels of low density lipoprotein (LDL) have been associated with higher cardiovascular disease risk while higher levels of high density lipoprotein (HDL) have been associated with lower cardiovascular disease risk. Therefore, the relative amounts of LDL and HDL to total cholesterol are more important than the total cholesterol itself (Willett, 1995). A 2% decrease in ischemic heart disease has been associated with a 1% lowering of blood cholesterol in middle aged men. Women who have low levels of HDL and high triglyceride levels have been associated with increased cardiovascular risk (Heart and Stroke Foundation of Canada, 1995).

Some 4% of men and 5% of women report having diabetes (Heart and Stroke Foundation of Canada, 1995). Diabetes (specifically diabetes mellitus) is a significant cause of death on its own (over 5,000 deaths in connection in 1993) but it is also a major risk factor for cardiovascular disease. Several risk factors are associated with diabetes including blood glucose, lipids, blood pressure and body weight.

3.3.2 Lifestyle / Behavioral

Lifestyle factors can be enabling, precipitating and/or reinforcing. Most of the risk factors in this category are theoretically modifiable. However the difficulty in actually changing these risk factors can be substantial (e.g. those with a genetic component).

3.3.2.1 Smoking

Smoking is the single largest modifiable risk factor for mortality in Canada. Smoking is responsible for earlier mortality from cardiovascular disease, many types of cancer [lung, mouth, pharynx, larynx, esophagus, pancreas, bladder, kidney and possibly uterine cervix and colon (Ames et al., 1995; Illing et al., 1995; Miller, 1995)] and respiratory diseases. Unlike several other risk factors where moderation is not associated with increased health risks, even moderate use of tobacco increases health risks. In addition the addictive nature of tobacco prevents many people from smoking infrequently.

Among Canadians over the age of 15 in 1990 an estimated 31% of males and 28% of females were current smokers. Back in 1965 the rates were approximately 60% for males and 38% for females. In 1990, Quebec had the highest level of current smokers (34%) and British Columbia the lowest (26%) (Health Canada, 1993). There are fairly strong differences in rates based on education and income which are discussed in their appropriate sections in the societal category.

Because of the tremendous influence of smoking on health, epidemiological studies of most risk factors must standardize (i.e. measure and quantitatively compensate) for the effects of smoking much like they do for age and sex. Sometimes studies will look at the effects on non-smokers only to avoid confounding.

Based on Nurses Health Study and Framingham Study, cessation of smoking is followed by a 50% reduction in cardiovascular disease risk within 1 year and reduction to the level of never smokers within 5 years (Heart and Stroke Foundation of Canada, 1995). However, the same reduction does not occur for some cancers:

> "... at least for lung cancer, and possibly other tobacco-associated lung cancers as well, the risk acquired by smoking remains at about the same level after cessation, and does not fall to normal. Thus even though many people have given up smoking, with benefits relating to no further increase in their risk, many cancers are now occurring in ex-smokers." (Miller, 1995, pg. 656)

Most estimates of health risks relating to risk factors are not available specifically for Canada. However, for smoking there have been several recent articles estimating the impact of smoking on health. Despite the large number of studies on smoking, there are currently no reliable estimates on the average number of years of life expectancy that are lost due to smoking.

Illing and Kaiserman (1995) used a variety of information to estimate smoking-attributable mortality (SAM) for Canadians in 1991 (Table 3.4). Direct evidence was used in addition to relative risks to help estimate the number of deaths for 22 smoking-related diseases. Additional evidence was used to estimate the number of deaths from fires and from passive smoking. While their figures report deaths down to an individual level, this occurs because calculated estimates were not rounded off in relation to the level of confidence in the predictions. At most, the figures should not be quoted with more than two significant figures (e.g. report a total of 41 thousand, not 41,408) and for most such estimates, only one significant figure is appropriate.

Table 3.4 Smoking-Attributable Mortality (SAM) by Disease Category, Canada, 1991

The report estimates that the SAM as a percentage of all deaths is approximately 26% for males and 15% for females. Separate estimates for Canada divided into regions were included for Atlantic, Quebec, Ontario, Prairies and British Columbia. For males the SAM percentage for the regions ranged from 22.9% (Prairies) to 30.2% (Quebec) and for females from 13.6% (Prairies) to 16.9% (British Columbia).

When these SAM percentages are compared to the percentage of smokers, the impact of smoking on smokers is highlighted. Even if all 60% of males smoked in the past, an SAM of 26% for all men implies that almost half of male smokers have their lives shortened because of their smoking. A similar conclusion could be made for females smokers.

Table 3.4 Smoking-Attributable Mortality (SAM) by Disease Category, Canada, 1991

Disease Category	ICD-9	Males	Females	Both
Adult Diseases (35+ yrs of age)		**27,646**	**13,172**	**40,818**
Neoplasms		*11,435*	*4,833*	*16,268*
Lip, oral cavity, pharynx	140-149	673	174	847
Esophagus	150	579	225	804
Pancreas	157	358	441	799
Larynx	161	355	90	445
Trachea, lung, bronchus	162	8,739	3,583	12,322
Cervix uteri	180	-	136	136
Urinary bladder	188	403	135	538
Kidney, other urinary	189	328	49	377
Cardiovascular Diseases		*11,003*	*5,390*	*16,393*
Rheumatic heart disease	390-398	41	56	97
Hypertension	401-405	123	134	257
Ischemic heart disease	410-414			
Ages 35-64		2,635	644	3,279
Ages 65+		3,769	2,037	5,806
Pulmonary heart disease	415-417	99	76	175
Other heart disease	420-429	1,231	871	2,102
Cerebrovascular disease	430-438			
Ages 35-64		401	351	752
Ages 65+		1,178	319	1,497
Atherosclerosis	440	467	473	940
Aortic aneurysm	441	762	259	1,021
Other arterial disease	442-448	297	170	467
Respiratory Diseases		*5,208*	*2,949*	*8,157*
Respiratory tuberculosis	010-012	21	11	32
Pneumonia/influenza	480-487	912	966	1,878
Bronchitis/emphysema	491-492	962	376	1,338
Asthma	493	61	65	126
Chronic airways obstruction	496	3,252	1,531	4,783
Paediatric Diseases (<1 yr of age)		**101**	**70**	**171**
Low birth weight	765	19	17	36
Respiratory distress syndrome	769	23	14	37
Respiratory conditions-newborn	770	17	12	29
Sudden infant death syndrome	798.0	42	27	69
Fire Deaths (all ages)		**54**	**31**	**85**
Passive Smoking Deaths		**66**	**268**	**334**
TOTAL		**27,867**	**13,541**	**41,408***
SAM crude rate per 100,000		**210.2**	**99.2**	**153.9**
SAM as % of all deaths		**26.4%**	**15.0%**	**21.2%**

Illing and Kaiserman, 1995, Table 1

* these estimates have not been rounded off in relation to the level of confidence in the predictions. At most the figures should not be quoted with more than two significant figures and for most such estimates only one significant figure is appropriate

Ellison et al. (1995) used a different method to estimate smoking attributable deaths in Canada (Table 3.5). They used population attributable risk from smoking and multiplied it by the total number of deaths from all causes to generate their estimate. This method assumes that all the excess deaths in smokers vs. non-smokers was due only to smoking. This assumption would overestimate the number of deaths if smokers have a greater number of non-smoking related risk factors, on average, than non-smokers (e.g. such as excessive alcohol consumption).

Table 3.5 Estimated (1991) and Projected (2000) Smoking-Attributable Deaths, Canada

Coincidentally both of these studies used 1991 for their estimate, making comparison of their results easier. Ellison et al. (1995) estimated 12% more male deaths in 1991 than Illing and Kaiserman (1995) but a similar number of female deaths.

Peto et al. (1992) used a cruder method to estimate mortality from tobacco in developed countries including Canada (Table 3.6). An indirect method was used which took age and sex specific lung cancer rates to estimate tobacco related deaths from other diseases as well.

Table 3.6 Deaths Attributed to Smoking, Canada, 1995

A recent report (Single et al., 1996) estimated that for 1992 approximately 33,500 deaths were attributed to smoking. Considering these estimates together with the earlier studies, the range of death attributed to smoking between the highest and lowest estimates is approximately +/- 15% (33,500 to 48,000) for similar years. This range provides a direct indication of the degree of uncertainty associated with what is likely the most thoroughly studied and fully characterized risk factors.

Villeneuve and Mao (1994) focused specifically on the probability of developing lung cancer based on smoking status of Canadians. They estimated that 17.2% of current male smokers will eventually develop lung cancer versus 1.3% of non-smokers. For females, 11.6% will eventually develop lung cancer versus 1.4% of non-smokers.

A survey by Stewart et al. (1995) of maternal smoking was conducted in 1983 and 1992 in the Ottawa-Carleton region. 28.5% of women were found to have smoked after the first trimester in 1983 compared to 18.7% in 1992. Gradients were observed by age, education, marital status and poverty. Pregnant women who smoke have a higher rate of

Table 3.5 Estimated (1991) and Projected (2000) Smoking-Attributable Deaths, Canada

Year	Males	Females	Both
1991	31,698	13,367	45,065
2000	30,359	16,551	46,910

Ellison et al., 1995, Table 3

Table 3.6 Deaths Attributed to Smoking, Canada, 1995

Age	Males		Females		Both	
	fraction dying (thousands)	%	fraction dying (thousands)	%	fraction dying (thousands)	%
35-69	14/36	39	7.0/21	33	21/57	37
70+	17/62	27	10/66	15	27/128	21
35+	31/98	32	17/87	20	48/185	26

Peto et al., 1992, Figure 1

miscarriage, still-birth, premature birth, babies below average weight and higher infant mortality soon after birth.

High alcohol combined with smoking cigarettes is linked to cancers of the mouth, larynx, esophagus and upper respiratory tract. Alcohol and smoking apparently act synergistically and greatly increase the cancer risk at these sites in relation to the summation of the risk from each factor alone (Doll et al., 1981).

Smokeless tobacco which has been gaining popularity in North America increases the risk of mouth cancers and may increase chance of heart attacks and strokes.

Second Hand Smoking

Second hand smoke, also called passive smoke, is what non-smokers can be exposed to. This consists of inhaled smoke which is subsequently exhaled and sidestream smoke which is smoke directly from the cigarette smoldering between inhalation by the smoker. While quantitative estimates of the health risks associated with smoking are well characterized, quantitative health risk estimates for second hand smoke are very uncertain, almost at the opposite end of the spectrum. Reason suggests that second hand smoke could be a health risk to non-smokers because the vast majority of time is spent indoors, second hand tobacco smoke contains the same noxious mix of chemicals as inhaled smoke and a substantial proportion of inhaled or sidestream smoke is released into the air for others to breathe. However, in relation to the overwhelming evidence on smoking, the evidence for second hand smoke is comparatively weak.

Because the mortality associated with passive smoking is relatively low, the most widely studied disease has been lung cancer which poses the highest relative risk for smoking. Case-control studies of married couples where one smokes and the other does not, have been commonly used to study this issue. The most widely quoted figure associated with second hand smoke is an analysis which estimated 3,000 lung cancer deaths in nonsmokers in the U.S. (U.S. EPA, 1993). This study also concluded that an estimated 150,000 to 300,000 annual cases of lower respiratory tract infections were associated with passive smoking and 200,000 to 1,000,000 asthmatic children have their conditions worsened by passive smoking. Illing and Kaiserman (1995) estimated over 300 passive smoking deaths in Canada, the majority occurring in females. The uncertainty in these estimates will be substantially greater than the +/- 15% uncertainty range apparent for total mortality estimates among smokers. Despite the high degree of uncertainty involved with the

numerical estimates for second hand smoke, this exposure dwarfs virtually any other source of indoor air pollution which individuals will experience in any non-occupational setting.

3.3.2.2 Alcohol

In a 1994 survey, 58% of adult Canadians reported they were current drinkers (at least one drink per month), 21% drank on occasion, 12% were former drinkers and 10% had never consumed alcohol (Statistics Canada, 1995b).

The health effects of alcohol are complicated because there are both negative and positive associations with mortality. Alcohol is involved in many types of fatal accidents, most notably motor vehicle (described in Section 3.4.5.3) and is involved in poisoning. In 1993 accidental poisoning with alcohol was associated with the deaths of 105 people (79 males, 26 females) (Statistics Canada, 1995a). Negative health effects include possible inflammation and cirrhosis of the liver and liver cancer (Ames et al., 1995). Alcohol is also a risk factor in suicide as well as contributing to the serious individual, domestic and societal problems of alcoholism. The latter are outside the scope of this study but must be recognized as substantial.

On the positive side, low to moderate alcohol consumption is associated with lower mortality from heart disease. Since the late 1970's studies started finding the consumption of alcohol associated with a decrease in mortality, specifically from heart disease. A famous study (St. Leger et al., 1979) which compared national rates for 18 countries of ischemic heart disease and wine consumption, showed countries with increased wine consumption had lower heart disease rates. While this study was an ecological study, the weakest type which is subject to ecological fallacy, hundreds of subsequent studies have generally found a lower rate of mortality from heart disease with moderate alcohol consumption. However, the beneficial effects apparently only apply to some people. The following quote from a recent study on women support similar findings in men on who benefits from alcohol consumption:

> "In conclusion, these findings indicate that for women as a group light-to-moderate alcohol consumption confers a significant overall survival advantage. Among younger women and those without risk factors for coronary heart disease, however, light-to-moderate alcohol consumption is not associated with a reduction in total mortality and heavier drinking is associated with a substantial increase in mortality. For older women and women with coronary risk factors, light-to-moderate alcohol consumption is

> associated with a reduction in total mortality, although with heavier intake mortality is increased:" (Fuchs et al., 1995, pg. 1250)

In pregnant women many medical people advise that no alcohol should be consumed. Alcohol can readily cross the placental barrier and high levels of alcohol consumption during pregnancy can lead to fetal alcohol syndrome in the baby.

3.3.2.3 Drugs

Mortality resulting from drugs can result from overdosing (poisoning) and hormonally related drug use. Information on poisoning is based on direct information (from death certificates) while the information on hormonally related drug use is based on epidemiological study.

In 1994, 71% of males and 83% of females reported using at least one prescription or over the counter medication in the previous month. Pain relievers (62%), cough or cold remedies (15%) and allergy medications (10%) were the most common (Statistics Canada, 1995b). Drug poisoning data is related to direct evidence which include data for poisoning from drugs, medications or biologicals. Poisoning was listed as cause of death for 681 people in 1993 of which 239 were identified as opiates and related narcotics. These figures do not include people who committed suicide using drugs.

An estimated 21% of women aged 15 - 39 used birth control pills in 1994 and 15% of women aged 45 and over used menopausal hormones (Statistics Canada, 1995b). With high hormonal dosage of oral contraceptives, risk of fatal and non-fatal myocardial infarction is estimated to increase 2-4 fold. However with lower dose preparations (those which now are used) the absolute increase in risk is small. On the positive side, oral contraceptives are associated with a lowering of ovarian cancer risk. However, concurrent smoking and oral contraceptive use substantially elevates the risk of myocardial infarction (Heart and Stroke Foundation of Canada, 1995). Postmenopausal estrogen replacement seems to provide a protective effect of 1/3 to 1/2 lowering of risk for fatal and non-fatal heart attacks. However, since estrogen replacement can increase risk of endometrial cancer it is recommended that low dose progestin be combined with the estrogen. An estimated 5,250 lives are saved annually per 100,000 estrogen users from 50-75, or 333 lives annually for ishemic heart disease and stroke per 100,000 estrogen users from 65-75 years (Heart and Stroke Foundation of Canada, 1995).

3.3.2.4 Nutrition

Nutrition and diet provide very important risk factors but they remain one of the most uncertain groups of factors. The main proof for nutrition being important are the large differences in international rates for various causes of mortality. With only using this information, other explanations such as genetic difference can confound interpretation. However, when people migrate to new countries, the disease and mortality patterns often begin to match those of the new country. While environmental factors play some role in these findings, many studies point to the importance of nutrition.

The abstract of a recent article on nutrition and health provides a good summary on the issue:

> "Many recent studies have implicated dietary factors in the cause and prevention of important diseases, including cancer, coronary heart disease, birth defects and cataracts. There is strong evidence that vegetables and fruits protect against these diseases; however, the active constituents are incompletely identified. Whether fat per se is a major cause of disease is a question still under debate, although saturated and partially hydrogenated fats probably increase the risk of coronary heart disease. One clear conclusion is that many individuals in the United States have suboptimal diets and that the potential for disease prevention by improved nutrition is substantial." (Willett, 1994, pg. 532)

Nearly 200 studies in the epidemiological literature show association of diet to cancer incidence, with great consistency. The lowest quarter of dietary intake has roughly twice the cancer rate for most types of cancer (lung, larynx, oral cavity, esophagus, stomach, colon and rectum, bladder, pancreas, cervix and ovary). However only 9% of Americans (likely similar values in Canada) eat the recommended level of two fruits and three vegetables / day (Ames et al., 1995).

The National Research Council in the U.S. provided a series of nine recommendations in its large report on diet and health which focused on chronic disease risk (National Research Council, 1989):

1. Reduce total fat intake to 30% or less of calories. Reduce saturated fatty acid intake to less than 10% of calories, and the intake of cholesterol to less than 300 mg daily. The intake of fat and cholesterol can be reduced by substituting fish, poultry without skin, lean meats, and low- or nonfat dairy products for fatty meats and whole-milk dairy products; by choosing more vegetables, fruits, cereals, and legumes; and by limiting oils, fats, egg yolks, and fried and other fatty foods

2. Every day eat five or more servings of a combination of vegetables and fruits, especially green and yellow vegetables and citrus fruits. Also, increase intake of starches and other complex carbohydrates by eating six or more daily servings of a combination of breads, cereals, and legumes.
3. Maintain protein intake at moderate levels.
4. Balance food intake and physical activity to maintain appropriate body weight.
5. The committee does not recommend alcohol consumption. For those who drink alcoholic beverages, the committee recommends limiting consumption to the equivalent of less than 1 ounce of pure alcohol in a single day. This is the equivalent of two cans of beer, two small glasses of wine, or two average cocktails. Pregnant women should avoid alcoholic beverages.
6. Limit total daily intake of salt (sodium chloride) to 6 g or less. Limit the use of salt in cooking and avoid adding it to food at the table. Salty, highly processed salty, salt-preserved, and salt-pickled foods should be consumed sparingly.
7. Maintain adequate calcium intake.
8. Avoid taking dietary supplements in excess of the RDA [recommended daily allowance] in any one day.
9. Maintain an optimal intake of fluoride, particularly during the years of primary and secondary tooth formation and growth.

The NRC (1989) concluded that there is not enough information to quantify the contribution of diet to the overall cancer risk or to determine the quantitative reduction that might be achieved by following any of the recommendations. They did note that among dietary factors the first recommendation, on reducing fat intake, is likely to have the greatest impact. Willett (1994) observes that the type of fat is important (monounsaturated or polyunsaturated preferable to saturated fat) and suggests that increased fruit and vegetable consumption could have a greater impact than lowering fat intake.

Miller (1992) provided an excellent overview of risk factors associated with cancer. The following are some population attributable risk (PAR) values Miller assigned to diet related factors for individual cancer sites (all estimates are based on males except breast):

- colorectal (60%) - reduce fat and increase vegetable consumption
- breast (27%) - reduce fat and increase vegetable consumption
- prostate (20%) - reduce fat consumption

- stomach (80%) - reduce nitrite in cured meats and salt-preserved foods, and increase fruit and vegetable consumption
- oral (10%) - increase fruit and vegetable consumption
- pancreas (30%) - reduce sugar and increase vegetable consumption
- kidney (30%) - reduce fat consumption
- ovary (30%) - reduce fat consumption

3.3.2.5 Exercise

In 1994, 56% of Canadians reported they were inactive in leisure time, 27% were moderately active and 17% had physically active leisure pursuits (Statistics Canada, 1995b). The category of physical activity was based on a calculation involving the average hours of physical duration and the energy cost of the activity. Another survey indicated that 43% of Canadians are considered inactive in their leisure time (Heart and Stroke Foundation of Canada, 1995).

Physical inactivity, whether occupational and recreational is associated with increased risk of CHD independent of other risk factors (WHO, 1994). Most is related to heart disease, with some to incidence of stroke (Heart and Stroke Foundation of Canada, 1995). Regular exercise is associated with lower blood pressure and less obesity which is linked to diabetes.

3.3.2.6 Weight

The body mass index (BMI) is often used as an index of an individual's weight. The BMI is a person's weight in kilograms divided by the square of their height in metres. In a 1994 survey of Canadians aged 20 - 64, 23% were overweight (BMI 28 and over), 23% had some excess weight (BMI between 25 and 27), 43% were in the acceptable range (BMI between 20 and 24) and 9% were underweight (BMI less than 20). Of those overweight, 25% were male and 20% were female (Statistics Canada, 1995b).

In an editorial in The New England Journal of Medicine, Byers (1995) gives his opinion on the current knowledge about the relation between body weight and mortality using three questions which he attempts to answer:

1. Is it harmful to be overweight? The answer is yes with some qualifications. Studies show an increase in mortality above a BMI 27. However differences occur between sexes and the area of the body where the fat is located

2. Within the range of "normal" weights, is it better to be thinner? The answer is no.
3. Does it matter if weight changes over time? The answer is yes and no. Over a few years loses and variation in weight may be harmful but small weight gains are not. However, over longer periods moderate weight change (+/- 10 kg) is not harmful but major weight gain (over 10 kg) is associated with increased mortality.

In a study on weight based on the Nurses Health Study cohort in the U.S., among non-smokers the relative risk of women with a BMI greater than 32 for cardiovascular diseases was 4.1 (95% CI 2.1 - 7.7) and for cancer was 2.1 (95% CI 1.4 - 3.2) compared to women with a BMI less than 19.

There is a strong association between nutrition, exercise, diabetes, high blood pressure, cholesterol level and smoking. Abdominal obesity is associated with increased risk of ischemic heart disease. Obesity and abdominal fat distribution are associated with an increased prevalence of diabetes, high blood pressure and elevated plasma cholesterol. The prevalence of high blood pressure is more than doubled among individuals with abdominal obesity (Heart and Stroke Foundation of Canada, 1995).

3.3.2.7 Sexual and Reproductive

Breast cancer is apparently hormonally mediated, with late age of first birth or no births being strong risk factors. Sexual and reproductive factors are also linked to endometrial, ovarian and cervical as well as colo-rectal cancer in women. Reducing the number of sexual partners and barrier contraception should reduce incidence of cervical cancer, while providing concurrent reduction of the risk of contracting AIDS (Miller, 1995).

3.3.2.8 Safety

Evidence of the toll of injury and death, particularly among young people, has promoted the development of a variety of safety devices, such as:

- motor vehicle - mode of transport, use of seatbelts, airbags, ABS, helmets (motorcycle and bicycle)
- medical - regular checkups, blood pressure and cholesterol levels (cardiovascular disease), pap tests (cervical cancer) , mammograms (breast cancer), digital rectal exam (prostate cancer)
- fire - smoke detectors, sprinklers, fire extinguisher
- recreational - life jackets, harnesses, protective clothing

- occupational - protective equipment, safety devices

An overriding theme relating to safety is the level of education. Most risks can be reduced with proper training in addition to safety devices. These include defensive driving courses, courses on potentially high risk recreational activities, occupational safety courses (e.g. WHMIS - workplace hazardous materials information system) and health courses (e.g. CPR - cardiopulmonary resuscitation)

3.3.2.9 Personality

> Those who Race toward Death
> Those who wait
> Those who worry
>
> Jim Morrison of "The Doors" (1943-1971)

The degree and frequency of risk-taking is related to personality. Some people continually take large risks while others avoid risks at all costs (which itself implies other risks are being taken inadvertently). However, most people are somewhere between. Most people often take high risks in some areas of their lives and avoid risks in others. Personality is one risk factor that could contribute to the high rates of motor vehicle accidents in young adults, the majority being male.

3.3.2.10 Stress

Stress is widely suspected to contribute to many health related factors. A difficulty in studying the effects of stress on health is that stress remains difficult to define and measure. Individuals in jobs that have a high demand but low individual control are at increased risk of cardiovascular diseases (WHO, 1994).

Increased stress is associated with an increased heart rate and respiration, elevated blood pressure, and elevated cholesterol and fat levels. In an effort to cope with stress, people may turn to alcohol and drugs with the risks they bring.

3.3.2.11 Multiple Risk Factors

This additional section is dedicated to looking at the effects of multiple lifestyle risk factors based on information from a large cohort study.

> "... we can control and modify our life span, the speed of ageing and the risk for major diseases simply by choosing an appropriate life-style." (Hirayama, 1990, pg. 1)

This quote is from a book summarizing the results of a cohort study in Japan that followed 270,000 adults aged 40 and above for 17 years (1966-1982). Unlike many prospective studies which focused mostly on smoking, the Japan study examined lifestyle issues as well.

Hirayama divided cause of death into cancer deaths and all other deaths. A total of 44 possible causes of death were analyzed. Seven lifestyle variables were examined, namely consumption of: meat, fish, milk, green-yellow vegetables, soybean paste soup, cigarettes and alcohol. Relative risks with 90% confidence intervals were calculated for each of the seven lifestyle variables comparing daily vs. non-daily exposure to each selected lifestyle variables. The choice of a 90% confidence level differs from the more conventional 95% confidence level which would demand a stronger association to conclude that any association was statistically significant.

Table 3.7 summarizes their calculations and lists for each lifestyle variable the number of causes of death that were significant at the 90% confidence interval level. Cigarettes were associated with an increased relative risk in 29 of the 44 possible causes of death analyzed. Green-yellow vegetables were associated with a decreased relative risk in 15 of the 44 possible causes of death and an increased relative risk in only one.

Table 3.7 Summary of Relative Risks for Lifestyle Variables Found to be Statistically Significant (10% Significance Level)

Table 3.8 shows mortality rates for people with different lifestyle variables (smoking, meat, green-yellow vegetables and drinkers). The absence or presence of a dot indicates whether or not the person is a daily user of the variable. The most significant but not surprising finding is that the mortality rate for non-smokers (#1-8) is lower than the mortality rate for all smokers (#9-16) indicating the significance of smoking to health. A less significant finding is that green-yellow vegetables lower the mortality rate, even in smokers.

Table 3.8 Age-Standardized Mortality Rates for Combinations of Lifestyle Variables

Table 3.7 Summary of Relative Risks for Lifestyle Variables Found to be Statistically Significant (10% Significance Level)

Daily Consumption of	RR Significantly	
	Below 1.0	Above 1.0
Cigarettes	0 of 44	29 of 44
Alcohol	3 of 44	18 of 44
Milk	8 of 44	10 of 44
Soybean Paste Soup	9 of 44	7 of 44
Meat	13 of 44	5 of 44
Fish	14 of 44	4 of 44
Green-Yellow Vegetables	15 of 44	1 of 44

Hirayama, 1990, Table 13

Table 3.8 Age-Standardized Mortality Rates for Combinations of Lifestyle Variables

#	Variable				# of Deaths	All Cancers	All Causes
	S	M	G	D		Age-Stdzd Rate	Age-Stdzd Rate
1					1,006	306	1,542
2				●	259	347	1,478
3			●		2,738	324	1,482
4			●	●	916	357	1,507
5		●			30	471	1,390
6		●		●	16	367	1,159
7		●	●		169	352	1,321
8		●	●	●	98	450	1,629
9	●				3,797	548	1,901
10	●			●	2,279	574	2,121
11	●		●		8,536	522	1,830
11	●		●	●	5,569	595	2,064
13	●	●			187	586	1,937
14	●	●		●	198	808	2,261
15	●	●	●		596	508	1,644
16	●	●	●	●	595	542	1,834

S - smoking, M - meat, G - green-yellow vegetables, D - drinking
Hirayama, 1990, Table 31

Smoking, alcohol and meat consumption actually shift the mortality rate upward at all ages by varying amounts. What this implies is that these habits do not only have an effect later in life, but also increase mortality earlier in life. However, because age is such a substantial risk factor, more people are affected later in life. The shift varies from 5-15+ year shift for selected causes. Eating green-yellow vegetables decreased the observed upward shift.

3.3.3 Societal

3.3.3.1 Education Level

Individuals with a lower level of education (<6 yrs of education) are more likely to have one major risk factor for cardiovascular disease than those with more (>=12 yrs of education), men 77% vs. 58%, women 86% vs. 53% (Heart and Stroke Foundation of Canada, 1995).

In a 1994 survey of Canadians' self reported health, 72% of people with a post-secondary or diploma education reported excellent or very good health while only 48% of people with less than secondary completion reported the same (Statistics Canada, 1995b). These results must be interpreted in relation to individual perception of how satisfied any individual is with their personal circumstances.

The estimated percentage of current smokers over age 15 according to individual maximum education level in 1990 was: elementary (34%), secondary (31%), college (27%) and university (18%) (Health Canada, 1993). Clearly, smoking prevalence is lower with higher level of attained education. This is likely to be a substantial contributor to any association between health status and education.

3.3.3.2 Economic Status

Socio-economic status is a widely studied risk factor, often in relation with education level and lifestyle/behavioural risk factors. An older report by Health and Welfare Canada looked at mortality by income level in urban Canada and concluded that:

> "Despite the problems which arise in the interpretation of differential mortality by income level, it is clear that Canadians in lower income levels

> did experience substantially higher mortality rates for most diseases than persons with higher incomes." (Health and Welfare Canada, 1980, pg. 3)

The association between economic status and health is widely accepted and a causal linkage is supported by a variety of evidence. Economic status, usually measured in the form of household or individual income, is the commonly used measure for dividing population into groups based on socio-economic status. Studies in several countries have shown that higher household incomes are associated with a declining annual mortality risk except at the highest incomes levels (Graham et al., 1992). Increased income is related to better nutrition, sanitation, health care and education (Keeney, 1990).

In a 1994 survey of Canadians' self reported health, 77% of males and 74% of females in the highest household income group reported excellent or very good health while 52% of males and 51% of females in the lowest income group reported the same (Statistics Canada, 1995b).

Two articles looked at mortality and other health outcomes relating to the income level of Canadians (Wilkins et al., 1989; Wilkins et al., 1991). The articles used the metropolitan areas of Canada which accounted for approximately 60% of the population and divided the areas by census tract into income quintiles (20% increments). Some of the results, based on 1986 information, were as follows:

- life expectancy of 5.6 years greater for males and 1.8 years greater for females in the highest compared to the lowest income quintile
- for males the age standardized mortality rates per 10,000 by income quintile (highest to lowest) were: q1 (57), q2 (60), q3 (64), q4 (69), q5 (86)
- for females the age standardized mortality rates per 10,000 by income quintile (highest to lowest) were: q1 (49), q2 (50), q3 (49), q4 (50), q5 (56)
- for males the relative ratio of higher mortality between the lowest and highest income quintiles for the major causes of death were: infectious (1.90), cancer (1.40), cardiovascular (1.35), respiratory (1.67), external (1.88) and for all causes (1.52)
- for females the relative ratio of higher mortality between the lowest and highest income quintiles for the major causes of death were: infectious (1.24), cancer (1.47), cardiovascular (1.11), respiratory (1.03), external (1.43) and for all causes (1.13)
- the rate ratio (relative risk) for infant mortality and low birth weight between the highest and lowest income quintiles were 1.7 and 1.4 respectively

In summary, there were consistent trends for several measures of health based on income level. These trends were strongest in males and were strongest for the lowest (poorest) income quintile.

The estimated percentage of current smokers over age 15 by income in 1990 is as follows: very poor (36%), other poor (32%), lower middle (34%), upper middle (29%) and rich (25%) (Health Canada, 1993).

Hirayama, who's work on lifestyle risk factors was summarized in section 3.3.2.11 downplayed the importance of socioeconomic factors:

> "In summary, although socioeconomic status is an important determinant of mortality from various causes of death, the influence of selected life-style variables on risk of dying from these causes is mostly independent of socioeconomic status." (Hirayama, 1990, pg. 120)

3.3.3.3 Race

Race is not recorded on death certificates in Canada. However, race is recorded in the U.S. and most vital statistics include information by race.

> "Vital statistics in the U.S. report information by race in addition to age and gender. ... In the U.S., blacks have a higher mortality rate for most causes. Rates of mortality in blacks are greater than twice that of whites for diabetes, hypertension, homicide, maternal mortality and infant mortality. These differences are related to many other risk factors including diet, lifestyle, education, occupations, access to and use of health care, etc." (Lilienfeld et al., 1994, pg. 93)

In Canada, the health of natives have been studied extensively because of their increased overall mortality. The mortality rate for natives is approximately two to four times greater for those under the age of 50 relative to the Canadian average. Once again, other risk factors related to societal issues including economic factors such as poor housing on reserves and other lifestyle/behavioural factors are the main reasons associated with high mortality among Canadian natives (Shah, 1994). Overall the linkage between poverty and race is inferential.

3.3.3.4 Unemployment

A good review of unemployment and health in Canada was conducted by Jin et al. (1995), who concluded that:

> "on an epidemiologic basis, the evidence suggests a strong, positive association between unemployment and many adverse health outcomes. Whether unemployment causes these adverse outcomes is less straightforward, however, because there are likely many mediating and confounding factors, which may be social, economic or clinical" (Jin et al., 1995, pg. 529)

The types of effects leading to adverse health effects from unemployment included the disruption of relationships, greater risk behaviour (alcohol consumption and poor diet), increased stress and by the precipitation of a bereavement reaction.

3.3.3.5 Marital Status

There is accurate evidence on marital status, based on direct evidence recorded from death certificates. This information was reviewed in Section 2.7 (Figures 2.18 and 2.19). The direct information showed that married people have death rates two to three times lower than single and widowed/divorced people. This was consistent between age categories and sexes.

The reasons behind this association are less well known. Single people may be less safety conscious than married people. Some insurance companies will often lower car insurance premiums for males under 25 who are married. Being widowed or divorced may increase financial and emotional stress. However, caution must be used in making conclusions since confounding occurs (e.g. chronic health problems may interfere with marriage and increase the death rate)

3.3.3.6 Occupation

Both accidental and chronic occupational risks will be considered. An idea of occupational mortality relating to accidents can taken from the Workmen Compensation Board data combined with estimates of employment by occupation (Statistics Canada, 1994; Statistics Canada, 1995c). Table 3.9 summarizes evidence for 1993. The year recorded is not necessarily the year the incident causing death occurred, rather it is the year during which the claim was accepted. However, barring large annual variations, the numbers should be similar. The overall annual mortality rate for occupational mortality relating to accidents was 7.3 deaths per 100,000.

Table 3.9 Occupational Mortality, 1993

Table 3.9 Occupational Mortality, 1993

Occupation	Annual Fatalities	Employment (thousands)	Mortality Rate (per 100,000)
Agriculture and related services	15		
Fishing and trapping	17		
Logging and forestry	50	74.4	67
Mining, quarrying and oil wells	106	118.1	90
Manufacturing	128	1636.1	7.8
Construction	137	484.2	28
Transportation and storage	107	452.3	24
Communication and other utilities	21	389.3	5.4
Wholesale trade	29	602.1	4.8
Retail trade	19	1366.3	1.4
Finance and insurance	3	479.1	0.6
Real estate operator and insurance agent	3	187.7	1.6
Business services	15	534.1	2.8
Government services	46		
Educational services	10	758.0	1.3
Health and social services	6	1149.8	0.5
Accommodation, food and beverage services	13	808.1	1.6
Other services	14		
Industry unspecified or undefined	19		
TOTAL	758	10369.2	7.3

Data Source: Statistics Canada, 1994a and 1995e

Identifying environmental carcinogens is a major area of study in public health sciences. As will be discussed in the Predictive Information section, entire disciplines are being devoted to identify environmental carcinogens. Characterizing any substance as a human carcinogen is a judgment which requires human evidence so that epidemiology is required. Currently, only a handful of environmental chemicals have been characterized as human carcinogens, with the evidence for most having been based on studies of occupational exposures. Half of 60 chemicals and mixtures which the International Agency for Research on Cancer (IARC) of the World Health Organization classified as carcinogenic in humans are based on occupational exposures (Ames et al., 1995). Occupational exposures allow better identification and characterization of individual exposures than other types of exposure. Likewise, occupational exposures generally involve higher levels of exposure than non-occupational exposures (Siemiatycki, 1992).

One of the earlier Canadian studies on occupation and mortality was by Howe and Lindsay (1983) who analyzed mortality information for approximately 10% of the Canadian workforce between 1965-73. While this was a weak epidemiological study for several reasons, including no data on confounders such as smoking, it did clearly show what has been termed the healthy worker effect. Overall this study group had a standard mortality ratio (SMR, a measure of relative risk) of 0.83 (90% CI 0.82-0.84) and for cancer an SMR of 0.88 (90% CI 0.86-0.90).

Doll and Peto (1981) estimated that occupation contributed to 4% of cancer. Rodricks (1992) noted that Doll and Peto have reduced their estimate for occupation to approximately 1%. However, Miller (1992) in a Canadian study, concluded that 9% of cancer deaths were attributable to occupation. Miller claims that Doll and Peto's estimates were too low because they eliminated the overlap with tobacco, yet occupation and tobacco use are interactive.

Siemiatycki (1992) has performed a large case-control study of occupational cancers in Montreal. Some of the sites of study included gastro-intestinal, lung, genito-urinary and lymphomas. For bladder cancer, which is the second most studied occupational cancer after lung, Siemiatycki et al. (1994) estimated that 6.5% (95% CI 2.0 - 9.9) of bladder cancers were attributable to occupational exposures.

3.3.3.7 Geographic Area / Region

In Canada it is common practice to supply information distinguished by province. As a risk factor, geographic location is generally weak. For cancer studies, provinces and governments have prepared cancer atlases that compare cancer incidence and mortality rates by geographic region (e.g. county). These are used to identify areas with abnormally high rates for a more detailed epidemiological study. Many differences between regions are linked to lifestyle/behavioural risk factors (e.g. lower smoking rates in western provinces).

3.3.3.8 Medical

The high quality of medical care in Canada has had advantageous results in reducing mortality and prolonging life. Some of the instruments used by the medical community to reduce health risks include: immunization, antibiotics, chemotherapy, surgery and radiation treatment.

We should recognize that in life-threatening situations, relatively high risks are taken compared to regular life, because of the anticipated benefit in overcoming the threat. For example, some cancer chemotherapeutic drugs, particularly alkylating agents cause secondary malignancies, most commonly leukemias, lymphomas, and sarcomas (Ames et al., 1995).

3.3.3.9 Transportation

This section will summarize the risks associated with various modes of transportation. In section 3.4.5.3, risk factors for motor vehicle accidents will be examined in more detail.

Table 3.10 summarizes some U.S. values for the risks of various modes of transportation. The number of deaths per 100 million miles traveled is shown in addition to the relative risk compared to the safest mode, which is bus travel. Walking and bicycles were not included for lack of data but the risk of these modes of transportation depend almost entirely on what other transportation they must mix with (i.e. most people who get killed walking or biking are struck by a motor vehicle) (Halperin, 1993).

Table 3.10 Risk by Various Modes of Transportation

Table 3.10 Risk by Various Modes of Transportation

Mode of Travel	Deaths / 100 million miles (Risk relative to safest mode)	
	Inter-urban	Intra-urban
18-year old males, no seat belts, intoxicated, driving light cars on rural interstates	49.0 (1600)	93.0 (9300)
Motorcycle (aggregate)	29.0 (970)	29.0 (2900)
Roadway/Automotive (aggregate)	2.1 (70)	2.1 (210)
Average drivers	0.67 (22)	1.3 (130)
40-year old females, wearing seat belts, sober, driving heavy cars on rural interstates	0.080 (2.7)	0.15 (15)
Airline passengers	0.061 (2.0)	
Train (Amtrak) passengers	0.052 (1.7)	
Bus passengers	0.03 (1.0)	0.01 (1.0)

Halperin, 1993, Tables 1 and 2

3.3.3.10 Recreational

Recreational activities are a good example of where the risk is partly associated with its enjoyment. Often an increased challenge is linked to an increased level of risk (e.g. canoeing on a lake versus canoeing down rapids).

Cohen (1991) summarized the risk of several recreational activities. Though based on U.S. data, the information is applicable to Canada. Cohen used loss of life expectancy (LLE) described in Section 2.9.6 in addition to probability to quantify the risks. Wilson and Crouch (1982) have comparable numbers for recreational activities.

Table 3.11 Risk Associated with Various Recreational Activities

3.3.3.11 Other

There are several risks which are significant in other parts of world, but fortunately not in Canada. These include wars, famine and epidemics. Though violence is a meaningful risk to life in Canada, it is significantly lower than in U.S.

3.3.4 Environmental

Environment is a word that has multiple meanings in different contexts. At one extreme the environment and genetics are the only factors that cause disease. Everything not already encoded in one's genes is the environment and the body is exposed to these factors through the air, food and water. Much confusion surrounds the intended meaning of environment in relation to health risk. However, for this thesis a much narrower definition of the environment is used. The environment is defined as the unintentional exposure to specific agents from the environment. One exception is drinking water which we intentionally drink, however, we do not intentionally consume agents which may be present in drinking water. There are four exposure routes which connect the environment and the human body: inhalation (air), eating (food), drinking (water), skin (several) (Hrudey et al., 1996).

People commonly separate environmental risks into two broad categories - natural and human. Natural risks includes natural disasters and chemicals originally present in the environment (e.g. arsenic in drinking water). Human risks includes man-made or mass produced chemicals including car exhausts, industrial emissions and pesticide use. Agent-specific environmental risk factors are generally weak and highly confounded by other factors.

Table 3.11 Risk Associated with Various Recreational Activities

Activity	Annual Probability of Death	Loss of Life Expectancy per year of Participation (days)
Mountain Climbing - dedicated	1 : 167	110
Mountain Climbing - all climbers	1 : 1,750	10
Hang Gliding	1 : 560	25
Parachuting	1 : 570	25
Sail Planing	1 : 1,710	9
Professional Boxing	1 : 2,200	8
Scuba Diving - amateur	1 : 2,400	7
Snowmobiling	1 : 7,600	2
Mountain Hiking	1 : 15,700	0.9
Football - college	1 : 33,000	0.6
Skiing - racing	1 : 40,000	0.5

Cohen, 1991, Table 7

3.3.4.1 Air Pollution

The following quote summarizes of some of the recent focus of epidemiology and air pollution:

> "Are small particles in the air killing people? Dozens of studies conducted in the past five years suggest that they are. Even more disturbing, the studies show statistical associations between airborne particulate matter (PM) and increased mortality and sickness, even at levels well within current national air quality standards. Although the implied risks to individuals are small compared with health factors such as smoking, they are large compared with typical environmental risks from toxic compounds and carcinogens in the air and water." (Reichhardt, 1995, pg. 360A)

Reichhardt's statement makes two important observations, that air pollution from particulate matter may be one of the largest environmental risks we face but that the risks are small compared to other health factors. There are still many uncertain issues associated with air pollution and mortality. Some important uncertainties include whether it is the particle itself or some other pollutant attached to the particles that cause the health problem, what is the biological mechanism, a lack of accurate individual and indoor/outdoor exposure data and what is the association between specific causes of death. Another is whether air pollution affects the mortality of healthy people or only those who are already weak and susceptible from other conditions. Therefore it may be that air pollution is linked with mortality at the end of life, but it may have relatively less effect on an individual's overall life expectancy.

Small particles are not the only air pollution consideration but have shown stronger associations with mortality than specific air pollutants like ozone, nitrous oxide, sulphur dioxide and carbon monoxide. Lipfert and Wyzga (1995) examined results from 31 (mostly time-series) epidemiological studies and estimated the joint daily mortality from various air pollutants is approximately 5% of daily mortality. Once again the association is with daily mortality rates being studied rather than lifetime mortality.

Mauskopf (1987) estimated the future number of cancers caused by asbestos exposure between 1985-2000. The estimate for the U.S. was approximately 1500 cases of cancer over the next 100 years and included occupational and non-occupational exposures as well as lung cancer and mesothelioma.

3.3.4.2 Water Pollution

The most direct health risk related to water pollution is in drinking water. A more indirect concern is for people who eat large quantities of fish from polluted water. In drinking water there are two general concerns.

Pathogens are not usually a health concern when water is provided full conventional treatment and adequate disinfection. However in some rural locations the adequacy of water treatment is questionable. Pathogens of concern include bacteria (e.g. *Campylobacter*), viruses (e.g. Norwalk), *Giardia* and *Cryptosporidium*. The latter two pathogens are protozoan parasites which challenge the adequacy of water treatment to a greater degree than the bacterial pathogens.

Some inorganic chemicals like arsenic are naturally present in water at elevated concentrations and can pose a high health risk. Chlorination byproducts from disinfecting drinking water are suspected to cause some forms of cancer. Other chemicals like aluminum sulphate are added to water during the treatment process.

3.3.4.3 Food Additives and Contaminants

Most of the work with food additives and contaminants has been with quantitative risk assessment which is discussed in Section 4. The main groups of food additives include processing aids, texturing agents, preservatives, flavoring and appearance agents and nutritional supplements. Because any food additives will affect humans directly they are very highly regulated. Similarly, residual pesticides are of concern but apart from occupational exposures their risks must be estimated using quantitative risk assessment (Amdur et al., 1991).

3.3.4.4 Chemicals

Vainio and Wilbourn (1993) have summarized the chemicals associated with human cancer. The summary is based on the International Agency for Research on Cancer (IARC) documents. Of 742 chemicals studied, 57 have been judged by panels of experts to be associated with human cancer and these are shown in Table 3.12. The relative risk of the different chemicals listed and especially the circumstances of exposure vary greatly (e.g. tobacco smoke and furniture and cabinet making). The public is only exposed to trace levels, if any, for all but the consumer products (tobacco, alcohol, and pharmaceuticals) listed.

Table 3.12 Chemicals Associated with Human Cancer

Bruce Ames is an award-winning biochemist who is noted for discovering the Ames test for mutagenicity which provides a means for rapidly testing substances for their mutagenic potential. He is controversial speaker on the issue of natural versus synthetic chemicals and has stated:

> "There are more natural carcinogens by weight in a single cup of coffee than potentially carcinogenic synthetic pesticide residues in the average U.S. diet in a year, and there are still a thousand known chemicals in roasted coffee that have not been tested." (Ames et al., 1995, pg. 5262)

3.3.4.5 Radiation

Risk factors for skin cancer include light skin and hair, tendency to sunburn, and possibly sunburning incidents as a child (Miller, 1995). Doll and Peto (1981) have estimated that UV light causes 90% of lip cancer, 50%+ of melanomas and 80% of other skin cancers. Macneill et al., have stated:

> "The only well established causal factor for melanoma is sun exposure. Severe, intermittent exposure increases the risk of melanoma while continued regular exposure produces no increase and may even reduce the incidence. This is presumably because the protection against UVR provided by natural tanning and skin thickening associated with continued exposure is sufficient to more than compensate for the carcinogenic effects of the UVR itself" (Macneill et al., 1995)

An other important type of radiation exposure for the public is radon. Ames (1995) claims that radon is likely the most important indoor air pollution concern. Based on estimates from underground miners radon exposure is likely to contribute to 15,000 lung cancer per year (in the U.S.), mostly in smokers due to synergistic effects. However, epidemiological studies of radon have failed to convincingly demonstrate any excess risk at domestic exposure levels (Letourneau et al., 1994).

3.3.4.6 Natural Disasters

Cohen (1991) summarized the risk of several natural disasters in the U.S. (Table 3.13). Canada will have similar values but they may be lower for some (e.g. hurricanes) and higher for others (e.g. excessive cold). Cohen used loss of life expectancy (LLE) described in Section 2.9.6 to quantify the risks.

Table 3.13 Risk Associated with Various Natural Disasters

Table 3.12 Chemicals Associated with Human Cancer

Type	Chemicals and Exposure Circumstances		
Agents	Aflatoxins	Methyl-CCNU	Oestrogens - nonsteroidal and steroidal
	4-Aminobiphenyl	Chromium [VI] compounds	
	Arsenic and arsenic compounds	Ciclosporin	Oral contraceptive - combined and sequential
	Asbestos	Cyclophosphamide	
	Azathioprine	Diethylstilboestrol	Radon and its decay products
	Benzene	Erionite	
	Benzidine	Melphalan	Solar radiation
	Chlornaphazine	Methoxsalen plus UV	
	Bis (chloromethyl) ether and chloromethyl methyl ether	MOPP	Talc containing asbestiform fibres
		Mustard gas	
		2-Naphthylamine	Thiotepa
	Myleran	Nickel compounds	Treosulfan
	Chlorambucil	Oestrogen replacement therapy	Vinyl chloride
Complex Mixtures	Alcoholic beverages	Coal-tar pitches	Soots
	Analgesic mixtures containing phenacetin	Coal-tars	Tobacco products - smokeless (chewing tobacco, oral snuff)
		Mineral oils - untreated and mildly treated	
	Betel-quid with tobacco	Shale-oils	Tobacco smoke
Exposure Circumstances	Aluminum production	Haematite mining (underground) with exposure to radon	Magenta - manufacture of Painter (occupation exposure as)
	Auramine - manufacture of		
	Boot and shoe manufacture repair	Iron and steel founding	Rubber industry
	Coal gasification	Isopropanol manufacture (strong-acid process)	Strong inorganic acid mists containing sulfuric acid (occupational exposure to)
	Coke production		
	Furniture and cabinet making		

Vainio and Wilbourn, 1993, Tables 2, 3 and 4

Table 3.13 Risk Associated with Various Natural Disasters

Natural Disaster	Loss of Life Expectancy (days)
Hurricanes	0.3
Tornadoes	0.8
Excessive Heat	0.6 - 0.7
Excessive Cold	1.0 - 2.1
Lightning	0.7 - 1.1
Floods	0.4
Earthquakes	0.2
Tsunami	0.15

Cohen, 1991, Table 8

Table 3.14 Worst Tornadoes in Canada

Date	Location	Deaths	Injured
1912, June 12	Regina	28	100s
1987, July 31	Edmonton	27	300
1946, June 17	Windsor to Tecumseh	17	100s
1888, August 16	Lancaster Town to Valleyfield, Quebec	9 - 11	14
1974, April 3	Windsor	9	30

Colombo, 1996, pg. 23

Table 3.14 summarizes the five worst tornadoes in Canada.

Table 3.14 Worst Tornadoes in Canada

Lightning deaths are the only natural disaster listed on a death certificate. For Canada the following number of people died after being struck by lightning: 1991 - 5, 1992 - 4, 1993 - 1, 1994 - 11. Note the variability from year to year despite the relatively constant size of the population. Other natural hazards that kill Canadians include forest fires and weather-induced accidents.

3.4 Risk Factors by Cause of Death

3.4.1 Infectious Disease

The direct evidence highlighted the significant decline in mortality that has taken place with respect to infectious diseases. Barrett (1992) identified four factors associated with the mortality decline: sanitary reforms, changing disease patterns, improved medicine and health care and improvements in living standards:

1. Sanitary Reforms. Aim is to reduce contact with infectious micro-organisms which requires knowledge of the conditions which promote spread. There are five major routes by which humans can be infected: water (cholera, typhoid), food (dysentery, gastro-enteritis), vectors / carriers (rabies, malaria, bubonic plague), air (pneumonia, respiratory tuberculosis) and personal contact (sexually transmitted diseases). Drinking water has proven the easiest to control with appropriate technological measures.
2. Changing Disease Patterns. Changes in nature of disease itself. Scarlet fever was minor then became a major cause of death and changed to become less of a threat.
3. Improved Medicine and Health Care. Was taken for granted that mortality decline in 19th century Europe was result of medical advances, however, now lively debate. Much more influential in recent declines in third world. Most of tuberculosis decline had taken place before introduction of antibiotics, but when introduced decline was greater. Diphtheria, however, was decreased following anti-toxin introduction and then significantly decreased following immunization. Smallpox the other major exception.
4. Improvements in Living Standards. Incidence of many diseases decline with rising standards of living. Nutritional status affects an individual's resistance to: influenza, pneumonia, bronchitis, diarrhea and tuberculosis.

HIV infection has several risk factors relating to how it spreads. These are through sexual contact, sharing contaminated needles, from an infected mother to her baby, transfusion of infected blood and accidental handling of infected blood. The first and second categories are the most common ways HIV is spread. The last two categories currently carry very small risks, though effects of tainted blood transfusion are still current. Unlike most other types of health risks, there are several easy safety measures which can significantly reduce the probability of developing HIV infection. These are through sexual practices (e.g. abstinence, monogamous relationship, safe sex practices) and not sharing needles.

3.4.2 Cancer

Risk factors for a particular disease or outcome are often labeled as sufficient or necessary. A sufficient risk factor is one which will inevitably produce or initiate a disease and often has several components. A necessary risk factor is one which must be present for a disease to develop. Vainio and Wilbourn describe the difficulty in the terms of sufficient and necessary factors in studying the causes associated with cancer:

> "In human cancer, there is probably no such thing as a 'sufficient' and 'necessary' cause; all what we are studying are 'contributory' causes, active in some stages of the multistep (and multifactorial) process of carcinogenesis ... Therefore, for pragmatic purposes, an agent is considered carcinogenic when a change in the frequency or intensity of exposure to the agent is accompanied by a change in the frequency of occurrence of cancer of a particular type(s) at a later time." (Vainio et al., 1993, pg. s4)

In 1981, Doll and Peto published a review of the causes of cancer that is still widely used as a reference 15 years later. Two earlier publications in the same journal where Doll and Peto originally published their article were similar though less comprehensive (Wynder et al., 1977; Higginson et al., 1979).

Doll and Peto (1981) submitted four pieces of evidence that some human cancer is avoidable:

1. Differences in Incidence Between Countries. Doll and Peto included a table that lists 19 common cancers with a cumulative incidence of greater than 1% in any area and then for each of the 19 causes listed the ratio of the highest to the lowest incidence rate. These ranged from a ratio of 6 to over 100 indicating that large geographic variations existed.
2. Changes in Incidence Following Migration. Studies have shown that cancer rates of immigrants to new countries have developed cancer rates similar to those of the population in the new country. This has been largely attributed to lifestyle (avoidable) factors and has tended to downplay the importance of genetics (at least between race). This trend is likely changing with the rapid advances in genetic typing which are illuminating the specific role of genes in cancer.
3. Changes in Incidence over Time. When rates of cancer incidence change in the same country, it indicates that external factors are affecting those cancers. In the United States the mortality rate from stomach cancer decrease 61% while the morality rate for lung cancer increased 148% between 1950-51 and 1975.

4. Identification of Causes. Avoidability of cancer can be demonstrated if specific causes can be identified. If a particular chemical is removed from an occupational setting and is followed by decreases in cancer, provide evidence of causation.

Doll and Peto identify luck as the determinant that separates the differences between the actual and expected outcome (based on observation and theory). They point out that luck plays a role in determining exactly which individual will develop any cancer. However, for the population as a whole this luck is averaged out and become negligible (i.e. not all heavy smokers get lung cancer).

Table 3.15 shows the summary of Doll and Peto's estimates. As mentioned in the occupation section, Doll and Peto's estimate for occupation has been reduced to approximately 1%.

Table 3.15 Percentage of Cancer Deaths Attributed to Various Different Factors

Miller (1992) has developed a list similar to Table 3.15 for Canada using more recent information. For the categories similar to Doll and Peto, Miller provided the following 'best' estimates:

- Tobacco - 29%
- Diet - 20%
- Occupation - 9%
- Alcohol - 6%
- Sexual Activity - 3% and Parity - 4%
- Sunlight and Radiation - 1% each
- Drugs - 1%

In addition Miller attributed 8% to family history. Unlike Doll and Peto, Miller did not propose an uncertainty range for his estimates but there is little reason to expect the uncertainty in his estimates would be less than those proposed by Doll and Peto. In Miller's study he also presented a table of his estimates for the potential effects of prevention or early detection on cancer incidence which is reproduced in Table 3.16. These estimates do indicate that a large fraction of cancers are potentially preventable.

Table 3.15 Percentage of Cancer Deaths Attributed to Various Different Factors

Factor or Class of Factors	Best Estimate	Range of Acceptable Estimates
Tobacco	30	25 - 40
Alcohol	3	2 - 4
Diet	35	10 - 70
Food Additives	<1	-5 - 2
Reproductive and Sexual Behaviour	7	1 - 13
Occupation	4	2 - 8
Pollution	2	<1 - 5
Industrial Products	<1	<1 - 2
Medicines and Medical Procedures	1	0.5 - 3
Geophysical Factors	3	2 - 4
Infection	10 ?	1 - ?
Unknown	?	?

Doll and Peto, 1981, Table 20

Table 3.16 Estimates of Potential Effects of Prevention or Early Detection on Cancer Incidence

A more recent study on breast cancer could only attribute an estimated 41% (95% CI 1.6% - 80%) of cases in the U.S. to the major risk factors: later age at first birth, nulliparity, family history of breast cancer and higher socioeconomic status (Madigan et al., 1995).

3.4.3 Cardiovascular Disease

There are several major risk factors relating to cardiovascular disease: blood pressure, hypertension, blood cholesterol (lipids, LDL, HDL), smoking, alcohol, weight, exercise, diabetes, stress, heredity, oral contraceptives (+ smoking), menopause (estrogen), previous heart attack and atrial fibrillation.

Since cardiovascular disease is the leading cause of death there has been extensive study of the risk factors. Strikingly however there are few overall quantitative prediction available which highlights the difficulty in providing them. One of the few predictions for cardiovascular disease estimated that as much as 30% of cardiovascular disease mortality is attributable to high blood pressure, 19% to diabetes, 17% to smoking and 15% to elevated serum cholesterol (Heart and Stroke Foundation of Canada, 1995).

It has been estimated that 54% of the decline in ishemic heart disease in North America is due to changes in lifestyle, 40% to medical intervention and 6% unexplained. Medical intervention is performed thousands of times annually for cardiovascular disease. In fiscal year 1992-93 there were 15,034 coronary artery bypass surgeries and 14,299 angioplasties and both are increasing in number (Heart and Stroke Foundation of Canada, 1995). In addition an estimated 65,000 Canadians have pacemakers.

A limiting factor in determining who is at high risk is the imprecision with which they can be detected. Screening for major risk factors (serum cholesterol, blood pressure and smoking) will leave undetected about half the individuals in the population who will develop cardiovascular disease (WHO, 1994).

3.4.4 Respiratory Disease

Smoking is one of the largest risk factors for non-cancer respiratory disease. Based on comparing estimates of smoking attributable mortality by Illing and Kaiserman (1995) with total deaths, approximately 50% of male and 35% of female respiratory disease deaths are related to smoking. Respiratory failure is often the result of lifelong cumulative damage to

Table 3.16 Estimates of Potential Effects of Prevention or Early Detection on Cancer Incidence

Cancer Site	Action	PAR	Potentially Preventable
Lung	Eliminate smoking	90%	60%
	Reduce occupational exposure to carcinogens	20%	
Colorectal	Reduce fat and increase vegetable consumption	60%	77%
Breast	Reduce fat and increase vegetable consumption	27%	70%
	Reduce obesity (postmenopausal women)	12%	
	Screen women aged 50 to 69	25%*	
Prostate	Reduce fat consumption	20%	78%
Lymphoma	Reduce exposure to herbicides and pesticides	?	86%
Bladder	Eliminate smoking and reduce dietary cholesterol	60%	73%
	Reduce occupational exposure to carcinogens	27%	
Body of the uterus	Reduce obesity	30%	82%
	Protective effect of oral contraceptives (ages 20-54)	28%	
Stomach	Reduce nitrite in cured meats and salt-preserved foods, and increase fruit and vegetable consumption	80%	52%
Leukemia	Reduce exposure to radiation and benzene	?	70%
Oral, etc.	Eliminate smoking and reduce alcohol	80%	68%
	Increase fruit and vegetable consumption	10%	
Pancreas	Eliminate smoking	40%	64%
	Reduce sugar and increase vegetable consumption	30%	
Melanoma of the skin	Reduce unprotected exposure to sunlight	20%	77%
Kidney	Eliminate smoking	40%	67%
	Reduce fat consumption	30%	
Brain	Reduce occupational exposure to carcinogens	?	70%
Ovary	Reduce fat consumption	30%	53%
	Protective effect of oral contraceptives (ages 20-54)	26%	
Cervix	Eliminate smoking	23%	62%
	Encourage use of barrier contraceptives	?	
	Screen women aged 20 to 69	60%	

Estimates are for males except for breast, body of uterus, ovary and cervical cancer.
*effect on mortality not incidence
Miller, 1992, Table 4

lung function. This is related to Figure 1.1, showing disability versus impairment, where impairment continues increases causing permanent disability and eventually death.

From the cause of death perspective, respiratory disease is often the underlying cause of deaths that could be considered 'natural'.

3.4.5 External Causes

External causes are different than other major causes of death. These deaths occur from fatal injuries, and because they occur rapidly the contributing causes are more easily determined. However, similar to other causes of deaths, multiple risk factors are often associated with external cause deaths. To round out the types of risk factors associated with health risk the two largest external causes of death are reviewed, suicide and motor vehicle accidents.

3.4.5.1 Suicide

Identifying risk factors for suicide is important because it can be used to educate others on what to look for. Risk factors for suicide include: depression, previous attempted suicide, substance abuse, stressful life events, perceived or actual lack of family support, rural (isolated) residence, exposure to media reports on suicide and alienation (Hayes, 1994).

Blumenthal (1990) identified five overlapping domains for suicide:

- psychiatric diagnosis - more than 90% of adults who commit suicide have an associated psychiatric illness
- personality traits - aggression, impulsiveness and hopelessness. The combination of antisocial and depressive symptoms
- psychosocial factors, social supports, life events, and chronic medical illness - these combined with a recent humiliating life experience
- genetic and familial factors - genetics of suicide may be independent of family history disorders such as alcoholism
- neurochemical and biochemical variables - under investigation whether there are biological variables associated with psychiatric and personality traits

3.4.5.2 Motor Vehicle Accidents

Though accidents are different from most other causes of death, Gordon (1949) demonstrated that accidents had similar properties to infectious disease and could be studied

using epidemiological methods (e.g. there are variations by: time, age, race, geographic distribution and socio-economic distribution). Millar (1995) and Riley (1989) have reviewed accidents in Canada, including information on motor vehicle accidents.

For the past 20 years there has been a reduction of over 50% in the annual number of motor vehicle fatalities. If the number of vehicles registered is factored in (a form of standardization) then the reduction has been approximately 70% (Transport Canada, 1995b). However, motor vehicle accidents remain an important cause of death, especially in young adult males.

Motor vehicle accidents are different than many other forms of accidents in that a large amount of information in addition to what is filled out on the death certificate is recorded. This additional information is taken and summarized on a provincial and then national level based on collision reports filled out by police. The national report published by Transport Canada is entitled Traffic Collision Statistics in Canada (Transport Canada, 1994). Some of the information included is: sex, age, province, time, light condition, road surface, road condition, road type, weather condition, place of occurrence (rural/urban), road user class, vehicle type, vehicle condition, vehicle maneuver, model year, driver condition, driver action, pedestrian action and pedestrian collision site.

Motor vehicle accidents are a good example where multiple risk factors can interact to produce fatalities. Table 3.17 shows risk factors separated into ones relating to the vehicle, human and road. In addition, the risk factors are separated into those occurring before, during and after an accident. This table highlights the many factors that can be involved in any motor vehicle accident, each with their own contribution to the final outcome.

Table 3.17 Risk Factors for Motor Vehicle Accidents

45% of fatally injured drivers in 1993 had used alcohol. For males alcohol use was involved in 50% of the cases while in females alcohol was involved in only 26% of the cases (Transport Canada, 1995a).

Table 3.17 Risk Factors for Motor Vehicle Accidents

	Vehicle	Human	Road
BEFORE (Primary prevention)	*Design* Stability Road holding Power Visibility Brakes Lights Tires *Maintenance* Regular service Competent mechanics Training of mechanics	*Drivers* Adequate training Psychology Attitude Physical fitness Fatigue Emotional stress Alcohol Drugs *Pedestrians* Training Awareness Physical fitness (age) Fatigue Emotional stress Alcohol Drugs	*Design and Construction* Carriageway Surface Visibility Intersections Corners Traffic control equipment Signs Maintenance
DURING (Secondary prevention)	*Design* Stability Braking efficiency Steering control Tires *Built-in protection* Strong passenger compartment 'Crumple zones' Triplex glass Seat belts Door locks	Reflexes Training Psychology Physical fitness	Weather State of surface Space Presence of 'escape route'
AFTER (Tertiary prevention)	*Design* Ease of ingress for rescue Fire resistance	Psychology Training (first aid) Medical and rescue services	Communications Space of access to accident

Rowland and Cooper, 1983, Table 7.8

3.5 Uncertainty

Compared to direct evidence, the uncertainty in epidemiology is much greater. Considering epidemiologic studies rely on direct evidence which has uncertainties of its own, any uncertainties in indirect evidence and inference will be additional to the uncertainty in direct evidence.

Uncertainties in epidemiology can be separated into random and systematic error.

Random error is the difference between the measured and the true population value due to chance alone. Three major sources are individual biological variation, sampling error, and measurement error. Random error can be reduced by increasing the size of the study and by using more careful and specific measurement of exposure and outcome.

Systematic error (or bias) is related to the methods used to perform the study. Many possible sources of systematic error exist but the principal types include selection bias, measurement bias and confounding. Selection bias occurs when people in the study have a consistent difference from those not included in the study. A common example in occupational studies is that workers are healthier on average than the rest of the population (healthy worker effect). Measurement bias includes errors in biochemical or physiological measurements and recall bias when self reporting of health conditions is involved. Confounding occurs when an important factor not considered in the study is unequally distributed between exposed and unexposed groups (e.g. different rates of smoking between exposed and unexposed). One of the WHO criteria for supporting causation was study design because some designs deal with systematic errors better than others. Cohort and experimental studies have the potential to achieve lower systematic errors.

Table 3.18 compares bias and confounding of ecological, cross-sectional, case-control and cohort studies in addition to the time and cost required. As indicated earlier, the type of study is one factor used in determining the strength of association.

Table 3.18 Comparison of Observational Study Designs

Often, greater weight is placed on confidence intervals and statistical significance than is warranted. Confidence intervals only account for the random error, not the systematic errors from bias and confounding. Many epidemiological studies ignore this fact when

Table 3.18 Comparison of Observational Study Designs

	Ecological	Cross-sectional	Case-control	Cohort
Probability of:				
- selection bias	NA	medium	high	low
- recall bias	NA	high	high	low
- loss to follow-up	NA	NA	low	high
- confounding	high	medium	medium	low
Time required	low	medium	medium	high
Cost	low	medium	medium	high

Beaglehole et al., 1993, Table 3.6

discussing the significance of their outcomes (Taubes, 1995). When a 95% confidence interval is used as the basis for statistical significance, there is a less than 5% chance that a statistically significant result will be identified when no true association is present. The more outcomes that are measured, the greater the likelihood of finding a statistically significant outcome. Specifying the hypothesis before performing a study is essential in this regard. Data dredging (i.e. looking for some kind of significant association) after all the data are collected is very likely to find at least one significant association. This concept of prior hypothesis is illustrated with the golf analogy. If you ask what is the probability that your drive will land on a blade of grass, depending on whether you are a better golfer than me, your probability of landing on any blade of grass is likely to be high. But if you specify in advance that you will land on any particular blade of grass, the probability is infinitesimal. This is most relevant for prospective cohort studies involving commitment to the hypothesis before anything has occurred. This becomes harder to argue for retrospective studies where people will argue that what has happened has happened and was not subject to your hypothesis so why can you not change your hypothesis to fit the observations.

Shlyakhter et al. (1993) attempted to estimate the systematic uncertainty using physical measurements from atomic and sub-atomic particle data. Original estimates of the physical measurements including the confidence intervals were compared to more recent, presumably more accurate estimates. By comparing the original estimates with the recent estimates they could verify whether the confidence intervals were sufficiently large to include current estimates approaching the true value. They found that the original confidence intervals were far too narrow and the actual range of the 95% confidence intervals should have been almost twice as large (instead of a z=1.96 the actual z was approximately 3.8) for measures as experimentally verifiable as those encountered in particle physics.

> "By analogy with physical measurements, the results indicate that the usual 95% confidence intervals in epidemiology and environmental studies should be expanded to account for unsuspected systematic errors." (Shlyakhter et al., 1993, pg. 310)

By comparison, epidemiological measures are far less amenable to verification than those in particle physics, so the case for larger confidence intervals is even more compelling in epidemiology.

Earlier in this indirect evidence and inference section it explained how the population attributable risk (PAR) is a more important indicator of public health than just relative risks. However, if a PAR is low but can be reduced fairly easily then it may be worth doing (e.g. installing signals at crosswalks). Other factors include cost, potential future effects and who is affected (voluntary vs. involuntary risks).

For an association to be causal it does not necessarily need to have a high relative risk. If exposures and effects can be measured accurately then even risk factors with low relative risks can have strong associations (e.g. the association between early age of child birth, a factor which is readily verifiable, and reduced breast cancer) (Taubes, 1995).

One important element in epidemiological studies is the accuracy of exposure estimates. Some, like age of first child for females, are very accurate. Estimates of smoking are less accurate but most people know approximately how many cigarettes or packs per day or week are smoked. Estimates for diet are usually very inaccurate. Can you remember what you ate last week? What was the fat content? What type of fat was it?

For environmental epidemiology, exposure estimates are a large part of the uncertainty. For carcinogens, estimates of exposure need to be made for 10, 20 or more years earlier. In a factory, processes change, different locations have huge differences in concentrations, etc. One of the basics of epidemiology and toxicology is the dose-response relationship that higher exposures should result in higher risk (e.g. more cigarettes smoked or more fat content in the diet or higher and longer exposure to carcinogens). If the exposure cannot be measured or estimated accurately, then the uncertainty of the estimates are increased. In particular, distinguishing exposed from unexposed or being confident about degree of exposure is often the critical limiting constraint in environmental epidemiology (Saunders, 1996).

4. PREDICTIVE INFERENCE

Predictive inference involves risk assessment and is based on toxicological studies of specific chemicals and compounds. Estimates of health risk to humans can be generated for certain types of chemicals. Predictive inference is used to help develop guidelines intended to protect human health by limiting exposure.

Predictive inference focuses on estimating the probability of developing cancer from long-term exposure to chemical carcinogens. Acute exposure to chemicals falls under direct evidence with poisoning being the main cause of death. Chronic exposure to chemicals was also covered under indirect evidence and inference, but this only covers a limited number of chemicals involving high exposures, usually occurring in occupational settings.

Risk assessment and toxicology are closely connected. The human health risk estimates are generated with the process of risk assessment which requires the use of toxicological information. Toxicology itself is regarded as both an art and a science (Amdur et al., 1991). The scientific elements are mainly associated with the observations and experimental evidence collected on the effects of poisons. The element of art refers to the interpretation of this evidence for purposes such as risk assessment.

While the uncertainties associated with predictive inference are enormous compared to indirect and especially direct evidence, predictive inference has several advantages. Because of the large component of common genetic code (DNA), there is a substantial link between effects in animals and human health effects. The laboratory environment allows many factors to be rigourously controlled thereby helping to establish causation between a chemical and an effect. Mechanisms of toxic action can be studied through invasive monitoring and post mortem examination. Laboratory experiments allows new drugs and chemical compounds to be tested before widespread human exposure arises. The tragic consequences of the drug Thalidomide could have been avoided if current laboratory procedures were used. From a pragmatic standpoint, risk assessment provides additional insight that can be useful in judging health risks. Despite the inherent and enormous uncertainties of predictive inference, no alternatives exist for predicting health risks before they are allowed to happen in human populations.

4.1 Risk Assessment

> "Risk assessment is the evaluation of the toxic properties of a chemical and the conditions of human exposure to it in order both to determine the likelihood that exposed humans will be adversely affected, and to characterize the nature of the effects they may experience" (ATSDR, 1990)

Risk assessment has been formalized into a four step process which is outlined in the following sections.

1. Hazard Identification

Hazard identification seeks to determine whether the chemical in question causes an adverse effect. Any available and relevant information from both epidemiology and toxicology is used to determine what associations may exist between exposure and effect for the chemical. Relevant effects include mortality, reproductive or developmental effects, neurotoxicity, specific organ damage and cancer (Amdur et al., 1991).

2. Dose-Response Assessment

Dose-response assessment seeks to determine the relationship between the dose of the chemical and the response in humans. This is often the most controversial aspect of risk assessment because data is rarely available for doses experienced by the general population. For a limited number of chemicals, data from human exposure, often occupational exposures, are available. In most cases, data from animal experiments must be used. In either case, extrapolations from high to low doses are required and this involves several assumptions which are discussed later. For the more common predictions derived from animal experiments, extrapolations from animal to humans are required.

3. Exposure Assessment

Exposure assessments seeks to determine the human exposure to the chemical in question. For many chemicals, no adequate exposure information is available for the general population which means no risk assessment can be performed unless exposure is estimated using models. Dimensions of exposure include intensity, frequency, schedule, route and duration, and the nature, size and makeup of the exposed population. Difficulties include competing exposures, interactions with other chemicals, and special populations (e.g. old, young, pregnant). Major exposure routes to humans are through the air, food and water (Amdur et al., 1991).

4. Risk Characterization

Risk characterization combines the dose-response and exposure assessments to estimate the incidence of the adverse effect in humans.

4.1.1 Risk Assessment Protocols

The risk assessment protocol for non-carcinogens estimates a reference dose, a dose below which adverse effects are not expected. However for non-carcinogens, no estimate of probability of harm is made for doses below this reference dose. Mortality from non-carcinogenic substances is usually the result of an acute, massive exposure. In such cases, observations would fall into direct evidence (poisoning). Therefore, a more detailed discussion of non-carcinogenic substances was beyond the scope of this thesis even though the guidelines/standards derived for non-carcinogens are a significant part of risk assessment research.

Current risk assessment protocols only perform a estimate of risk probability for carcinogens. These quantitative estimates will be the focus of discussion in this section of the thesis.

4.2 Toxicology

Toxicology is the art and science concerned with adverse effects of chemical agents on biological systems.

There are three main professional categories of toxicologists: descriptive, mechanistic and regulatory. Descriptive toxicologists perform toxicity testing on experimental animals. This information is used to evaluate risks to humans and the environment. Mechanistic toxicologists study the mechanisms of action of the toxic effects. The regulatory toxicologists use the data provided by the descriptive toxicologists and evaluate the risk associated with a chemical.

This section on toxicology will focus on descriptive toxicology. Section 4.3 on interpreting cancer data focuses on regulatory toxicology.

4.2.1 Chemicals

Chemicals can be classified into three categories: elements, compounds and mixtures. Elements are the simplest form of matter and 90 elements have been discovered in nature and 18 more have been made. Most of these elements are rare. Compounds are substances formed by two or more elements which always combine in the same proportions (e.g. a water molecule is the same everywhere in the world). These compounds are formed by a chemical reaction and often have properties which are very different from the elements on their own. Mixtures can have variable compositions (e.g. the amount of sugar in coffee) and can be homogeneous (same properties throughout) or heterogeneous (two or more properties can be found throughout).

Toxicological risk assessment has only been able to focus on specific compounds and sometimes elements. Unfortunately, actual human exposure always involves a mixture of compounds and elements, hundreds and thousands of different chemicals in different concentrations.

With all this focus on chemicals it is important to remember how everything on earth, even our own bodies, are comprised of chemicals (Brady et al., 1988):

- air - is made of 78% nitrogen, 21% oxygen, carbon dioxide, argon and then traces of other gases

- surface of the earth - two thirds is covered with water made up of hydrogen and oxygen
- earth's crust - 47% oxygen, 28% silicon, 8.1% aluminum, 5.0% iron and then a variety of other elements. Oxygen is so common because it bonds with other elements.
- human body - 62.8% oxygen, 19.4% carbon, 9.3% hydrogen, 5.1% nitrogen, 1.4% calcium and then a variety of other elements

The properties of chemicals influence how they interact with the environment and organisms. Some of the properties include the melting and boiling points, electrical conductivity, acidity/alkalinity, density, specific gravity, volatility, reactivity, partitioning coefficients and bioaccumulation potential.

There are an estimated 70 to 75 thousand chemicals in commercial use with over 40 thousand used in commercially significant quantities (Health and Welfare Canada, 1991). About one thousand new or replacement chemicals are being introduced each year. Most commercial chemicals will contain one or more biologically significant impurities. These chemicals are in addition to large numbers of naturally occurring chemicals that are not commercially used.

4.2.2 Some Principles of Toxicology

A fundamental concept in toxicology is that the dose makes the poison. Any chemical given in a large enough dose is harmful and capable of causing death. However, the range of doses required to cause death for different substances varies enormously.

One measure of the range is the dose required to cause death in half (50%) of the exposed animals (LD_{50}). This is typically measured in milligrams (mg) of the chemical divided by the bodyweight of the animal. Ethyl alcohol has a LD_{50} value of 10,000 (mg/kg) while botulinum toxin a LD_{50} value of 0.00001 mg/kg, a range of 9 orders of magnitude (1,000,000,000 fold). Clearly in evaluating the risk of any substance, two pieces of information are required: the toxicity of the substance (e.g. LD_{50} for acute toxicity) and the level of exposure (the actual dose administered).

There are several toxic effects from chemicals in addition to death and cancer. These include reproductive effects (fertility, birth defects or teratogenic), neurotoxic effects, immune system effects and damage to specific organs of the body like the liver and kidneys. Effects can also be distinguished according to whether they are immediate vs.

delayed, reversible vs. irreversible, local vs. systematic. For some types of effects a tolerance can be developed.

Some chemicals are essential to the function of the body and harm is caused when their dose is too low. Chemicals can interact with each other in a variety of ways: additivity, synergism, antagonism and potentiation.

4.2.3 Absorption, Distribution, Metabolism, Excretion

When performing a risk assessment, the exposure to a human is usually determined by the concentration in the air, food or water. However, what actually happens to the human (or animal) when exposed to a substance varies tremendously depending on the chemical, the exposure scenario, the species and the individual. The process that a chemical goes through upon entering the body are absorption, distribution, metabolism and excretion. These processes help explain the differences in effect for different chemicals, for the same chemical in different species and for differences within a species.

Absorption is the amount of chemical that crosses an exchange boundary in an organism. The three main exchange boundaries are the gastrointestinal tract, the lungs and the skin. It is possible for substances to enter the body or touch the skin without causing consequences if they are not absorbed. An exception would be if they are irritants that affect the point of contact. The gastrointestinal tract is the organ where substances in food and water are absorbed into the blood stream. Many factors affect the amount of a chemical that is absorbed, including the nature of the chemical (e.g. solubility, pH, ...) and the species of animal. Differences exist between individuals within the same species (variability).

A chemical is distributed throughout the body in the bloodstream following absorption. Once in the bloodstream the substance can move to various parts of the body. Depending on the chemical it may be stored in fat tissue or in the bone. Two natural barriers exist in the body. These are the blood-brain barrier which prevents many non-essential chemicals from entering the brain, and the placenta, which separates the mother from the developing fetus.

Once in the bloodstream the chemicals can be metabolized by several organs. The liver is the main metabolic organ but the skin, lungs, intestines and kidneys also metabolize chemicals. Metabolism is performed by enzymes which change the chemicals into metabolites. Often the metabolism of non-essential chemicals changes them into

metabolites which promote excretion of the chemical from the body. In some cases, the metabolism actually creates metabolites that are more dangerous than the original chemical. Efficiency of metabolism is a significant factor for differences in effects of chemicals between individual and species.

Excretion takes place through the urine, feces and exhaled air and to a lesser extent through sweat and saliva. As mentioned, for the fecal and exhalation excretion routes the chemicals may have never been absorbed into the body. In other cases, excretion involves transfer back from the blood stream (e.g. alcohol in exhaled breath).

4.2.4 Types of Toxicological Investigation

Experimental toxicology studies the adverse effects of chemicals on health and the conditions under which those effects occur. Generally animal bioassays are used to determine dose-response relationships for specific chemicals or mixtures. Bioassays range from short term acute testing to long term chronic testing. Adverse effects monitored depend on the substance being tested.

There are three general types of toxicological investigations (Amdur et al., 1991):

1. animal bioassays -three main types based on length of duration, acute, subchronic and chronic. Acute bioassays use high doses over short time and are used to determine clinical signs of toxicity or types of adverse reactions and potency. Acute bioassays have little relevance to chronic or low level human exposures but they are useful for characterizing high level exposures and for selecting doses for longer-term studies. Subchronic bioassays generally range from 1 to 3 months and are used to determine likely effects for longer term chronic studies. Finally chronic bioassays are greater than three months in duration and include cancer bioassays which typically last the majority of the test animals lifespan (e.g. two years in rodents).
2. genotoxicity studies - short-term studies have been developed to measure genetic and chromosomal mutations in bacteria, fungi, plants, insects, cultured mammalian cells, or small mammals
3. metabolic and pharmacokinetic studies - measure rate of absorption, distribution and elimination. These compare test results from different species and help determine how much chemical actually reaches the target organ and to differentiate between external level of exposure and the dose of chemical which actually reaches the tissue where effects may be caused.

4.2.5 Cancer Bioassay

The following is an attempt to highlight some of the decisions and procedures involved in conducting a cancer bioassay. The results of a cancer bioassay form the base for extrapolation to humans. Although performing a cancer bioassay is a rigorous scientific exercise, the design of the bioassay has been based on both scientific principles and a range of policy choices.

Good laboratory practices have been developed. These include a protocol stating the purpose of the study, how it will be achieved, list of staff and their qualifications. Procedures are required for care of the animals including cage washing, temperature maintenance, humidity, lighting and weighing animals. Additional procedures are required for preparing slides and performing pathological assessments of the tissue (e.g. cancer). Both an internal and external group monitor the performance of a bioassay. Several million pieces of data can be generated from these studies and a single study can cost approximately 2.5 million dollars (Health and Welfare Canada, 1991).

A brief review of the design of a cancer bioassay is presented to highlight the complexity and difficulties involved. Nine areas involved in the design of the bioassay are outlined below (Health and Welfare Canada, 1991):

1. Test Chemical. The chemical used in the bioassay is customarily the same as that to which the public will be exposed. The chemical must be checked for any impurities which may be known or suspected carcinogens. The protocol must ensure that animals are exposed only to the intended chemical and not products of decomposition or other impurities.
2. Choice of Animal Species and Strain. Routinely, two animals species are used. In practice rats and mice are most commonly used. Hamsters, dogs and primates can be used, but in the case of dogs and primates a very long, and thus expensive, experiment is required. One problem with rats and mice is that they have a high incidence of naturally occurring cancer in some tissues.
3. Routes of Administration of the Test Chemical. The dosage route should resemble the major route of exposure found in humans. Routes include water, food ingestion, air inhalation, skin (painting) and injection into the blood stream or intraperitoneal cavity. The dosage route affects the amount and distribution of the chemical in the animals body.
4. Dose Selection. A major problem in a chronic cancer bioassay involves selecting the maximum tolerated dose (MTD). This dose must be the maximum possible dose that does not produce substantial non-tumour effects, affect the longevity of the animals or reduce the

animals weight greater than 10% compared to the controls. Subchronic studies of 90 days or less are normally performed to establish the MTD. The danger in only selecting doses well below the MTD is that a carcinogenic effect may actually be caused by the substance but may not be observed within the limited test population at the maximum dose tested. Frequently two additional doses are used at 1/2 and 1/4 of the MTD in addition to the controls.

5. Number of Animals to be Used. Usually 50 animals of each sex are used for the chemical with an equal or greater number of control animals. The number of animals used is a compromise between providing useful information and affordability of the entire procedure.

6. Diet. Different types of diet can be used. In cancer bioassays, the animals are usually allowed free access to their food. A dilemma is that restricting access to food reduces the amount of cancer and increases the animals longevity, but questions are now being raised about the role of excess feeding in causing cancer.

7. Avoidance of Bias. Even though animals are genetically similar, differences exist, and randomization is used in selecting animals for the different doses of the chemical. The location of the cages can be periodically and randomly switched to avoid biases like lighting and drafts. In addition, keeping animals in separate cages avoids competition over food supply which can alter the formation of tumours (e.g. restricting access to food as mentioned above)

8. Study Duration. The study must cover an appreciable proportion of the animal's lifetime, enough to allow cancer before otherwise natural death. Two years are used for rats and one and a half to two years for mice. Over the past decade, laboratory rat strains have on average increased their body weight and concurrently experienced decreased longevity.

9. Special Protocols. Additional areas of study can be added to the bioassay. One of the most difficult is a two-generation study where animals are exposed to a chemical for two months or more, then mated, and the offspring raised in a similar manner to the conventional bioassay. A different study design can be done to test whether the chemical is a tumour promoter.

Other factors to consider in the animal bioassay are the care of animals, the postmortem examination and pathological examination of tissues and the statistical analysis.

4.3 Interpreting Cancer Data

Once the animal data has been generated it must then be interpreted. There are three key issues associated with using animal data to predict human effects. There are whether or not a threshold exists, extrapolating from a high to low dose and comparing animals to humans.

4.3.1 Threshold vs. Non-Threshold

One of the most controversial debates in risk assessment is whether or not carcinogenic chemicals have a threshold in their dose-response relationship. If there is not a threshold, then any exposure to a carcinogen poses some risk even if the risk is negligibly small. Theoretically, a single molecule of a carcinogenic substance could under the ideal circumstances react with DNA in a cell to produce a mutated cell which can subsequently replicate and lead to a cancerous tumour.

The following example illustrates the no threshold hypothesis. Assume that one million people are randomly scattered along an elevated ledge that is 100 m wide and that falling off the ledge causes a person to develop cancer. If everyone must move toward the edge 90 m from where they were standing, 90% (or 900,000 people) get cancer. However, if everyone must move toward the edge only 1 m, 1% (or 10,000 people) get cancer. Even if the distance for moving toward the edge is reduced to 1 mm, 0.001% (or 10 people) get cancer. No matter how small the distance, there is always a probability that someone will develop cancer, even if the probability is less than one person.

A cautious and protective policy involves the assumption that carcinogenic chemicals do not have a threshold. From a scientific perspective, some chemicals show no measurable evidence of a threshold while many other chemicals do show evidence of a threshold. Because it is not possible to prove a negative, it is not possible to scientifically prove the absence of a threshold. However, assuming no thresholds does not mean that no 'safe' level of exposure exists because safety does not equate with zero risk (Hrudey et al., 1995).

Several issues are involved:

- mechanistic data - it is widely accepted that there are several stages involved in the development of cancer from chemicals. The two basic stages are initiation and promotion and chemicals can be classified as either or both. Theoretically, only

initiators should be able to have no threshold while promoters should exhibit a threshold

- animals studies - because most animals studies involve testing only 50 animals at two or three doses, they are not capable of answering the threshold debate. These studies can only detect effects at 10% probability of response. However a large study involving a total of over 23,000 mice was used to observe the shape of the dose-response curve down to the 1% response level. The results were inconclusive because the development of bladder tumours seemed to indicate a threshold but the liver tumours did not (Amdur et al., 1991)
- repair mechanisms - the human body has about 10^{14} cells with $4x10^9$ bases per cell which go through 10^{16} division cycles in a normal human life. The estimated error rate for DNA replication is about 10^{-10} mutations per base pair per cell generation. Therefore, the natural spontaneous errors are usually many times greater compared to the probability of injury from very low level exposure to environmental chemicals (Koshland Jr., 1994)
- everyone on this planet has detectable level of known carcinogens in their body (environmental carcinogens have been found at the north and south poles). A fundamental premise of chemistry is that Avogadro's number is $6.02x10^{23}$ molecules per mole of a pure substance (e.g. 1 mole of sugar is 358 g and will contain $6.02x10^{23}$ molecules of sugar). So while it is possible from a philosophical point of view to talk of zero risk, in reality (assuming that no threshold exists) everyone is at risk from chemicals in the environment. If everyone is at some low level of exposure then the question should be what is the level of risk, not is there a risk?

4.3.2 Extrapolation from High to Low Dose

Regardless of whether or not carcinogenic chemicals have thresholds, extrapolation is required because the doses experienced by humans are usually several orders of magnitude smaller than the lowest dose given to animals. Even when human exposure data is available, the concentrations commonly experienced by the public are significantly lower than the human exposures (usually occupational) found in the studies and extrapolation is required.

There are two basic types of models: statistical or distribution models and mechanistic models. Statistical or mechanistic models assume a threshold below which no response will occur. Some of these models include the log-probit, Mantel-Bryan, logit and Weibull.

Mechanistic models usually assume no threshold exists but can incorporate multiple hits or multiple stages of carcinogenesis in their calculations. Some of these models include the one-hit, gamma multihit, linearized multistage and stochastic two-stage. While the mechanistic models can be based on conceptual mechanisms, none are currently based upon measurement of contributing mechanistic parameters, rather, they seek to fit observed patterns or response in the animals bioassays. Consequently, their mechanistic basis is still empirically applied and their extrapolation is inherently uncertain.

The most widely used method of extrapolation from animals has been the linearized multistage model (U.S. EPA, 1986). A key assumption with the model is that there is no threshold, or no-effect level, for exposure to a carcinogen. An important point to remember with predictive inference is that it seeks to be cautious in nature. Usually, no attempt is made to make a best estimate of the risk. As the EPA put it:

> "It should be emphasized that the linearized multistage procedure leads to a plausible upper limit to the risk that is consistent with some proposed mechanisms of carcinogenesis. Such an estimate, however, does not necessarily give a realistic prediction of the risk. The true value of the risk is unknown, and may be as low as zero." (U.S. EPA, 1986, pg. 33997)

One additional factor that makes this procedure conservative is that the most sensitive of the study results are used for the extrapolation. Even within rodents species, differences in potencies of several orders of magnitude can occur from the same exposure.

The model generates a linear slope from zero dose up towards the actual animal exposure data. The slope of this line is known as the q_1^* or the potency slope value. The steeper the slope, the more potent the carcinogen is. Not all potency slope values are calculated using the linearized multistage model. When a dose-response relationship can be derived from human epidemiology studies (e.g. inorganic arsenic, benzene, cadmium) other methods of extrapolation are used to estimate the potency value. However, for most chemicals and substances, quantitative human epidemiological studies are not available.

These potency slope values are often translated into a unit risk factor. This involves selecting a life time risk level, typically one in a million and using the q_1^* values together with default assumptions about intake rates (breathing rate or water ingestion) to calculate an environmental medium concentration which would correspond to the specified risk level.

4.3.3 Interspecies Comparisons

A concern in toxicological risk assessment is the validity of using laboratory animals to calculate the risk to humans. In a review of genetically related (phylogenetic) animal studies, only a 74% agreement on observed carcinogenicity has been observed. Obviously, experimental animals and humans are not genetically identical and it raises concerns on the validity of these comparisons. However, nearly all chemicals showing human carcinogenicity based on epidemiological studies have ultimately been found to be carcinogenic in animals (Health and Welfare Canada, 1991)

Some differences between animals and humans are:

- life span - rodents typically have life spans of 2 or 3 years vs. over 75 for humans
- genetic homogeneity - laboratory animals are bred to be genetically similar
- body mass and size - mass of human is 3500 times greater than that of a mouse, while surface area is only about 390 times greater - approximately a 10 fold difference in ratios
- metabolic processes and rates - much higher metabolic rates in rodents and
- exposure - is the route of exposure used in the animal study similar to human routes?

One interesting similarity between rodents and humans is the probability of developing cancer over their lifetime. Both have a cumulative cancer risk that increases with age to approximately the fourth power. Approximately 30% of rats and mice will have cancer by the end of their 2 to 3 year lifespan (not tested with any chemicals or killed prematurely) (Ames, 1989). Humans have a 30% of developing cancer by the age of 80 (33% in males, 28% in females) (National Cancer Institute of Canada, 1996).

4.3.4 Other Methods

While the focus of this predictive inference section is on quantitative risk assessment, other methods are being used to evaluate cancer data. Two of these methods are the Human Exposure dose / Rodent Potency dose (HERP) index and the exposure/potency indices (EPIs). While both methods result in a quantitative estimate they do not provide an estimate of the risk probability to humans. They can be used as guides for comparing the results for several different chemicals.

The HERP index as it name suggests compares an estimate of human exposure to rodent potency (in the form of the TD_{50}) expressed as a percent. This method was developed by Ames, Magaw and Gold (1987) as an alternative to quantitative risk assessment which the authors argued was not scientifically credible because of the numerous uncertainties. They point out that their index is not a direct estimate of the human hazard but can be used to rank relative priorities of concern with regard to carcinogens.

The EPIs is currently used by Health Canada to characterize risk for carcinogens. The potency in this case is the "concentration or dose which induces a 5% increase in the incidence of, or deaths due to, tumours or heritable mutations considered to be associated with exposure" (Meek et al., 1994, pg. 114). The potency is based either on epidemiological studies or more commonly cancer bioassays. A dose-response model is required to estimate the 5% level but the uncertainties are small compared to the high to low dose and the animal to human extrapolations.

4.4 Exposure

Once the toxicological information is available, human exposure information is required before the risk assessment can be completed. While obtaining exposure information conceptually should be much easier than performing a toxicological investigation on a chemical, the amount of valid exposure information is suprisingly limited. So, just as there is a lack of toxicological information for many chemicals there is also a lack of exposure information.

There are many factors involved in estimating exposure to humans including:

- population - size, age structure, gender, special risk groups
- exposure pathways - groundwater, surface water, soil, air food chain, sediments
- exposure routes - ingestion, inhalation, dermal contact
- populations at risk - activity, location, age, high risk populations (elderly, pregnant women, infants, hypersensitive individuals, personal habits), magnitude and frequency of exposure
- exposure estimation - concentration, duration, frequency, fluctuation, bioavailability

Most of the reliable exposure information has been obtained for occupational settings. These exposures are usually greater than the general populations exposure which makes exposure easier to detect and monitoring a specific workforce is usually more practical than monitoring the entire population. Often, exposure information for the general population relies on a few measurements in one or two urban centres. Usually, only point estimates of exposure are available even though large variabilities exist with time and location. Ideally, some personal monitoring information is available in addition to general monitoring of environmental media (air, water, food), but this is rarely the case.

4.4.1 Exposure vs. Dose

Distinguish between exposure and dose is important. Exposure refers to the contact with the outer boundary of the organisms and is expressed in terms of a concentration. Dose however has several possible definitions including exposure. Rhomberg (1995) provided several definitions based on increasingly smaller but more relevant levels of dose as it is absorbed, metabolized and reaches the target organ dose:

1. Exposure -> applied dose and never consumed
2. Applied dose -> absorbed dose and not absorbed
3. Absorbed dose -> metabolized dose and not activated
4. Metabolized dose -> target organ dose and not reaching target organ
5. Target organ dose

4.5 Risk Estimates

Risk estimates provided in this discussion are made for only one small part of risk assessment. They can only be done for chemicals classified as carcinogens, which have a potency factor (which implies suitable toxicological or epidemiological data exists and a model was used to extrapolate the data) along with some estimates of human exposure. All of these requirements can be met for only a small number of chemicals.

4.5.1 Exposure

Accurate data on levels of human exposure is difficult to find. To provide an example, a quantitative risk assessment for Canadians, suitable exposure information was required. Instead of selecting chemicals at random, or attempting to gather all suitable exposure information in Canada the chemicals reviewed under the Canadian Environmental Protection Act (CEPA) provided a useful summary of exposure information for chemicals of potential concern.

CEPA was proclaimed in June of 1988 with the authority for the Ministers of the Environment and Health to investigate substances that may cause adverse effects on the environment or human health.

One of the conclusions for each CEPA study on any chemical or substance was whether or not the substance was 'toxic'. 'Toxic' for this legal purpose was assigned according to three categories:

a) harm to the environment,
b) danger to the environment on which human life depends, or
c) danger to human life or health.

In February 1989 the first Priority Substances List was published with 44 substances (later reduced to 43). All assessments were required to be published within 5 years from the publication of the list, a feat that was accomplished. 41 reports were prepared (dioxin and furans and Bis (Chloromethyl) Ether and Chloromethyl Methyl Ether were each combined into one report). These reports have been used as well as a summary of 35 of the substances in the journal Environmental Carcinogenesis & Ecotoxicology Reviews for (Meek et al., 1994) for preparing the following summary.

Table 4.1 is a summary of the 41 reports showing their classification for human toxicity, their carcinogenicity and whether or not there was exposure data. Only two of the chemicals classified as toxic did not have exposure data, benzidine and mineral fibres.

Table 4.1 Summary of CEPA Chemicals for Toxicity, Carcinogenicity and Exposure Data

Health Canada adopted the assumption of no threshold for carcinogens and automatically classified a substance that was a level I or II as 'toxic' to humans. Noteworthy, of the 41 reports, 15 reported being toxic for humans (category c) and all 15 were carcinogens of level III or greater (not all level III carcinogens were classified as toxic). Therefore, no non-carcinogens were classified as toxic. Of more concern was the carcinogen rating. Since potency values are only generated for carcinogens, only those chemicals given a rating of I, II and III were considered. The uncertainty may be considered to increase from I to III.

The exposure evidence which was collected was meant to be an average representative for the general population of Canada. The first criteria in selecting which chemicals to be used for quantitative calculations was the presence of exposure data. Of the 41 CEPA reports 27 contained some form of exposure data. Most of the exposure data was in the form of tables but for two chemicals (3,3'-Dichlorobenzidine and Methyl Methacrylate) the data was presented in the text.

The second criteria in selecting chemicals to be used was the carcinogenicity of the chemicals. Of the 27 reports with exposure data only chemicals with a carcinogenicity rating of I, II or III were selected. These criteria reduced the number chemicals to 17.

The seventeen chemicals were reduced to ten for the following reasons:

- chlorobenzene, 1,4-dichlorobenzene, nickel, styrene and trichloroethylene were withdrawn from the Integrated Risk Information System (IRIS) database for further review or were not available, so potency values were not available
- dioxins and furans were removed because of the difficulty of having exposure data in toxic equivalents and there was no equivalent IRIS data
- polycyclic aromatic hydrocarbons were not included because for the species to be evaluated, benzo[a]pyrene, the exposure data was for air while the IRIS database only contained potency values for oral ingestion

Table 4.1 Summary of CEPA Chemicals for Toxicity, Carcinogenicity and Exposure Data

#	Chemical	Tox	Carcinogen	Exposure Data
1.	Aniline	◆	III	No
2.	Arsenic and its Compounds	■	I (inorg)	Yes
3.	Benzene	■	I	Yes
4.	Benzidine	■	I	No
5.	Bis(2-Chloroethyl) Ether	◆	-	No
6.	Bis(2-Ethylhexyl) Phthalate	■	III / IV	Yes
7.	Bis(Chloromethyl) Ether and Chloromethyl Methyl Ether	-	I	No
8.	Cadmium	■	II (inorg)	Yes
9.	Chlorinated Wastewater Effluents	◆		No
10.	Chlorinated Paraffins	◆	II / III / VI	No
11.	Chlorobenzene [monochlorobenzene]	-	III	Yes
12.	Chromium and its Compounds	■	I (hex)	Yes
13.	Creosote-impregnated Waste Materials	◆		No
14.	Di-*n*-Octyl Phthalate	◆	VI	No
15.	Dibutyl Phthalate	-	VI	Yes
16.	1,2-Dichlorobenzene	-	V	Yes
17.	1,4-Dichlorobenzene	-	III	Yes
18.	3,3'-Dichlorobenzidine	■	II	Yes (text)
19.	1,2-Dichloroethane	■	II	Yes
20.	Dichloromethane	■	II	Yes
21.	3,5'-Dimethylaniline	◆		No
22.	Dioxins and Furans	■		Yes
23.	Hexachlorobenzene	■	II	Yes
24.	Inorganic Fluorides	-	-	Yes
25.	Methyl Methacrylate	-	VI	Yes (text)
26.	Methyl Tertiary-butyl Ether (MTBE)	-	VI	No
27.	Mineral Fibres (Man-made Vitreous Fibres)	■	II / III / IV / VI	No
28.	Nickel	■	I	Yes
29.	Non-pesticidal Organotin Compounds	◆		No
30.	Pentachlorobenzenes	-	VI	Yes
31.	Polycyclic Aromatic Hydrocarbons	■	II	Yes
32.	Pulp Mill Effluents	-		No
33.	Styrene	-	III	Yes
34.	Tetrachlorobenzenes	-	IV	Yes
35.	1,1,2,2-Tetrachloroethane	◆	III	Yes
36.	Tetrachloroethylene	-	IV	Yes
37.	Toluene	-	IV	Yes
38.	Trichlorobenzenes	-	VI	Yes
39.	Trichloroethylene	■	II	Yes
40.	Waste Crankcase Oils	◆		No
41.	Xylenes	-	IV	Yes

Environment Canada, CEPA documents

Toxicity
- ■ Toxic
- ◆ Inadequate Information
- - Not Toxic

Carcinogenicity Related to Humans
- I Carcinogenic
- II Probably Carcinogenic
- III Possible Carcinogenic
- IV Unlikely to Be Carcinogenic
- V Probably Not Carcinogenic
- VI Unclassifiable with Respect to Carcinogenicity

Exposure information was divided into three categories: food, drinking water and air. Nine of the ten chemicals had tables of the estimated daily intake broken into several age groups. The estimated daily intake values for food are shown in Table 4.2. It should be noted that in most cases the largest daily intake takes place during the early years and only using the 20-70 year age category would underestimate the mean intake over 70 years. Therefore, for the oral category, the estimated intake for food was taken as the weighted mean over the age categories. In the case of hexachlorobenzene this more than doubled the mean compared only to that for intake 20-70, because of the much greater estimated intake in the early years of life.

Table 4.2 Estimated Daily Food Intake by Age Categories

For both drinking water and air the estimated intake was not compatible with the potency factors which are expressed in concentrations to the negative power. Therefore, the concentrations (μg/L for drinking water and $\mu g/m^3$ for air) were taken from the footnotes to the estimated intake tables. Because concentrations do not change with age, no adjustments or additional calculations were required.

Table 4.3 Exposure Values

Several simplifications were made in selecting the exposure values for calculations in this thesis:

- only estimates for the general population were used (some chemicals has separate tables if living near a point source)
- soil/dirt exposure were not used, however, the daily intake from soil/food exposure was less than the daily intake from food
- only indoor air was used (in all but one case the indoor air had a higher concentration and overall exposure was greatest indoors since it was assumed 20 hours per day were spent indoors). In addition some chemicals had a separate listing for smoking which contributed significantly to the daily intake. However, for simplicity these additional exposure variables were not included in the calculations

Table 4.2 Estimated Daily Food Intake (µg/kg.bw/day) **by Age Categories**

#	Compound	Age Categories (years)				
		0 - 0.5	0.5 - 4	5 - 11	12 - 19	20-70
1.	Arsenic (inorganic)	0.2	0.3	0.2	0.1	0.08
2.	Benzene	0.06	0.06	0.05	0.03	0.02
3.	Bis(2-Ethylhexyl) Phthalate	7.9	18	13	7.2	4.9
4.	Cadmium	0.62	0.64	0.51	0.29	0.21
5.	Chromium (VI)	<0.9	<1.0	<0.7	<0.4	<0.3
6.	3,3'-Dichlorobenzidine					
7.	1,2-Dichloroethane					
8.	Dichloromethane	0.03	0.11	0.09	0.05	0.05
9.	Hexachlorobenzene	0.21	0.018	0.0098	0.0048	0.0027
10.	1,1,2,2-Tetrachloroethane					

Environment Canada, CEPA documents

Table 4.3 Exposure Values

#	Compound	Food (µg/kg.bw/day)	Drinking Water (µg/L)	Air (µg/m^3)
1.	Arsenic (inorganic)	0.11	5	0.0005 - 0.017
2.	Benzene	0.027	1	7.4
3.	Bis(2-Ethylhexyl) Phthalate	6.8	1 - 3	3.1
4.	Cadmium	0.28	<0.01 - 0.09	0.001 - 0.004
5.	Chromium (VI)	<0.4	0.3 - 4.3	0.003 - 0.009
6.	3,3'-Dichlorobenzidine	-	3.4E-10	7.6E-16
7.	1,2-Dichloroethane	-	<0.05 - 0.139	0.1
8.	Dichloromethane	0.06	0.2 - 2.6	16.3
9.	Hexachlorobenzene	0.0061	0.0001	0.00015
10.	1,1,2,2-Tetrachloroethane	-	0.05 - 1	0.1 - 0.25

Environment Canada, CEPA documents

4.5.2 Potency

Potency data was taken from the IRIS registry which contains reviews of toxicity data for several hundred chemicals. Each review is separated into four sections:

I - Chronic Health Hazard Assessments for Noncarcinogenic Effects

II - Carcinogenicity Assessment for Lifetime Exposure

III - Health Hazard for Varied Exposure Duration

IV - U.S. EPA Regulatory Actions

For this thesis, section II was the most important because it contained the carcinogenic slope potency estimates. These were contained in two subsections, the first on oral exposure which contained the oral slope factor and drinking water unit risk and the second on inhalation exposure which contained the inhalation unit risk. The IRIS registry was assessed on CD-ROM at the Alberta Environmental Protection library in Edmonton. The data was current to April 1996.

Table 4.4 presents the slope factors for the 10 chemicals selected from the CEPA documents. As mentioned, several chemicals have been withdrawn from the database for further review or were not available. While the slope factors for the withdrawn chemicals were available using the U.S. Agency for Toxic Substances and Disease Registry documents it was judged inappropriate to use any values currently under review or deleted from the IRIS registry.

Table 4.4 Slope Factors

Table 4.5 summarizes the basis for the slope factors shown in the previous table. Four of the ten chemicals were actually based on human data for their extrapolation (arsenic, benzene, cadmium and chromium) and used several different models. All but the oral arsenic value for these four chemicals was based on occupational exposures. The other six chemicals were based on rodent data and used the linearized multistage model for extrapolation.

Table 4.5 Basis for Slope Factors

Table 4.4 Slope Factors

#	Compound	Carcinogen (see below)	Oral $(mg/kg/day)^{-1}$	Drinking Water $(\mu g/L)^{-1}$	Air $(\mu g/m^3)^{-1}$
1.	Arsenic (inorganic)	A	1.5E+0	5E-5	4.3E-3
2.	Benzene	A	2.9E-2	8.3E-7	8.3E-6
3.	Bis(2-Ethylhexyl) Phthalate	B2	1.4E-2	4.0E-7	NA
4.	Cadmium	B1	NA	NA	1.8E-3
5.	Chromium (VI)	A	NA	NA	1.2E-2
6.	3,3'-Dichlorobenzidine	B2	4.5E-1	1.3E-5	NA
7.	1,2-Dichloroethane	B2	9.1E-2	2.6E-6	2.6E-5
8.	Dichloromethane	B2	7.5E-3	2.1E-7	4.7E-7
9.	Hexachlorobenzene	B2	1.6E+0	4.6E-5	4.6E-4
10.	1,1,2,2-Tetrachloroethane	C	2.0E-1	5.8E-6	5.8E-5

A. Known Human Carcinogen
B1. Probable Human Carcinogen
B2. Probable Carcinogen
C. Possible Human Carcinogen
D. Not Classifiable as to Human Carcinogenicity
E. Evidence of Non-carcinogenicity in Humans

U.S. EPA, IRIS database, June 1996

Table 4.5 Basis for Slope Factors

#	Compound	Type	Extrapolation Method	Tumour type, Test animals and Exposure Route
1.	Arsenic (inorganic)	Oral	Time- and dose-related formulation of the multistage model	Skin cancer Human (Taiwanese) Drinking water
		Inhalation	Absolute-risk linear model	Lung cancer Human (occupational) Inhalation
2.	Benzene	Oral	One hit (pooled data)	Leukemia Human (occupational) Inhalation
		Inhalation	One-hit (pooled data)	Same as above
3.	Bis(2-Ethylhexyl) Phthalate	Oral	Linearized multistage procedure, extra risk	Hepatocellular carcinoma and adenoma Mouse, male Diet
		Inhalation	NA	NA

Table 4.5 Basis for Slope Factors (Continued)

#	Compound	Type	Extrapolation Method	Tumour type, Test animals and Exposure Route
4.	Cadmium	Oral	NA	NA
		Inhalation	Two stage; only first affected by exposure; extra risk	Lung, trachea, bronchus cancer deaths Human (workplace) Inhalation
5.	Chromium (VI)	Oral	NA	NA
		Inhalation	Multistage, extra risk	Lung cancer deaths Human (occupational) Inhalation
6.	3,3'-Dichlorobenzidine	Oral	Linearized multistage procedure, extra risk	Mammy adenocarcinoma Rat, female Diet
		Inhalation	NA	NA
7.	1,2-Dichloroethane	Oral	Linearized multistage procedure with time-to-death analysis, extra risk	Hemangiosarcomas Rat, male Gavage
		Inhalation	Linearized multistage procedure, extra risk	Same as above, assuming 100% adsorption and metabolism at the low dose
8.	Dichloromethane	Oral	Linearized multistage procedure, extra risk	Hepatocellular adenomas or carcinomas and hepatocellular cancer and neoplastic nodules Mouse, male and female Inhalation and drinking water
		Inhalation	Linearized multistage procedure, extra risk	Combined aenomas and carcinomas Mouse, female Inhalation
9.	Hexachlorobenzene	Oral	Linearized multistage, extra risk	Hepatocellular carcinoma Rat, female Diet
		Inhalation	Linearized multistage, extra risk	Same as above
10.	1,1,2,2-Tetrachloroethane	Oral	Linearized multistage procedure, extra risk	Hepatocellular carcinoma Mouse Gavage
		Inhalation	Linearized multistage procedure, extra risk	Same as above

U.S. EPA, IRIS database, June 1996

4.5.3 Results

The calculation of the results is mathematically very simple. The risk, expressed as the lifetime risk of developing cancer, is calculated by multiplying the estimated average exposure by the slope factor. Table 4.6 summarizes these calculations which used exposure values from Table 4.3 and slope factors from Table 4.4. To help in interpreting the results, the results can be expressed as ratios (e.g. 1.6E-4 is the same as 1 in 6100). To calculate the annual risk the reported values must be divided by 70.

Table 4.6 Lifetime Cancer Risk

A more useful way to interpret these cautious estimates of lifetime cancer risk is to calculate the annual number of predicted cancers. By dividing the Canadian population by 70, there are on average 400,000 people in each age category (assuming a fixed stable population of 28 million who all live 70 years - the population is currently greater than 28 million and the life expectancy is greater than 70 years). Therefore, multiplying the values in Table 4.6 by 400,000 provides an estimate of the maximum likely annual number of predicted cancers for each chemical. These are shown in Table 4.7.

Table 4.7 Maximum Likely Annual Number of Predicted Cancers

Several assumptions have been made in generating this table. The sole purpose for these numbers is to compare and contrast them with estimates from the direct and indirect evidence sections. Even though the estimates in Table 4.7 are relatively low, it is important to remember that they are made with a method design to provide cautious estimates so the expected risks are likely to be much lower.

Table 4.6 Estimated Lifetime Cancer Risk

#	Compound	Oral (Food)	Drinking Water	Air
1.	Arsenic (inorganic)	1.6E-4	2.5E-4	2.2E-6 to 7.3E-5
2.	Benzene	7.8E-7	8.3E-7	6.1E-5
3.	Bis(2-Ethylhexyl) Phthalate	9.6E-5	4.0E-7 to 1.2E-6	
4.	Cadmium			1.8E-6 to 7.2E-6
5.	Chromium (VI)			3.6E-5 to 1.1E-4
6.	3,3'-Dichlorobenzidine		4.4E-15	
7.	1,2-Dichloroethane		1.3E-7 to 3.6E-7	2.6E-6
8.	Dichloromethane	4.3E-7	4.2E-8 to 5.5E-7	7.7E-6
9.	Hexachlorobenzene	9.8E-6	4.6E-9	6.9E-8
10.	1,1,2,2-Tetrachloroethane		2.9E-7 to 5.8E-6	5.8E-6 to 1.4E-5

Based on values from Tables 4.3 and 4.4

Table 4.7 Maximum Likely Annual Number of Predicted Cancers

#	Compound	Oral (Food)	Drinking Water	Air
1.	Arsenic (inorganic)	66	100	0.86 to 29
2.	Benzene	0.31	0.33	25
3.	Bis(2-Ethylhexyl) Phthalate	38	0.16 to 0.48	
4.	Cadmium			0.72 to 2.9
5.	Chromium (VI)			14 to 43
6.	3,3'-Dichlorobenzidine		1.7E-9	
7.	1,2-Dichloroethane		0.052 to 0.14	1
8.	Dichloromethane	.17	0.017 to 0.22	3
9.	Hexachlorobenzene	3.9	0.0018	0.028
10.	1,1,2,2-Tetrachloroethane		0.12 to 2.3	2.3 to 5.8

Based on multiplying values in Table 4.6 by 400,000

Note: this table attempts to quantify the annual number of cancers from lifetime exposure to estimated background levels of this compounds. These calculations do not include special consideration for individuals at greater exposures (i.e. occupational or other special circumstances).

4.6 Uncertainty

Different assumptions in risk assessments can change the risk probability estimates by several orders of magnitude. Differences in estimates based on which model is selected for the high to low dose extrapolation can be very large. One article compared four types of model for estimates at a 10^{-6} risk level. The most extreme differences was between the one-hit and the multihit model. For vinyl chloride the multihit model estimated a risk 2×10^{8} times smaller than the one-hit model. For nitriloacetic acid the multihit model estimated a risk 4×10^{5} times greater than the one-hit model (Food Safety Council, 1980).

Another example of the uncertainty is a risk assessment of N-nitrosodimethylamine (NDMA) to develop a drinking water guideline value. Four separate risk assessments were performed by different agencies, all using the same animal bioassay data (ACES, 1992). Three different models were used to estimate the potency slope factor. Of these three models, the highest estimate was 80 times greater than the lowest. After considering further reasonable assumptions, the difference between the highest and lowest proposed guideline value was over 5000 fold. This range provides an indication of the uncertainty possible for interpreting the same toxicological information from a single cancer bioassay for a specific chemical.

The uncertainties in predictive inference far exceed those of indirect evidence and inference, and they dramatically exceed the uncertainties of direct evidence. However, predictive inference has an important role despite its inherent uncertainty. Because of the controlled experimental conditions evidence of causation can, at least in theory, be obtained and the biological mechanisms of toxic action can be determined. Unlike direct and indirect evidence gathering which relies on measuring the effects of past exposures, predictive inference allows estimates of outcomes prior to human exposures (for new drugs and chemicals). Likewise, the predictive approach seeks to evaluate levels of risk far lower than those which can be measured using epidemiological approaches. However, the substantive meaning of the quantitative risk probability predications at extrapolated low doses remains controversial.

5. DISCUSSION

The three previous sections have summarized three bodies of health risk information. Direct evidence is based on information collected from individuals, and direct mortality evidence is based on death certificates. Indirect evidence and inference is based on information collected from individuals which is analyzed for causal inferences using epidemiological methods. Predictive inference is largely based on information from experimental animals studies which are extrapolated to estimate human health risk. Quantitative predictive estimates of mortality are currently only made for carcinogenic chemicals using toxicological risk assessment.

5.1 Comparisons Between Categories

5.1.1 Direct to Indirect

Many studies generating indirect evidence and inference rely upon direct evidence, in addition to other information. An example is the (Illing et al., 1995) study which used cause of death from the International Classification of Disease (ICD) codes and relative risks from a cohort epidemiological study to estimate smoking attributable mortality. Direct evidence provides the base for all health risk estimates.

5.1.2 Direct to Predictive

There is very little tangible relationship between direct evidence and predictive inference. Both are used to estimate the health risk from chemicals. For direct evidence, an example would be acute accidental or intentional poisoning by chemicals based on historical observations. Estimating the number of accidental poisonings this year would be based on the most recent poisoning data plus historical poisoning data. For predictive inference, the risk estimates are based on exposure relative to chronic (70 year) exposure to chemical carcinogens. Health risk estimates are based on knowledge of exposure concentrations and chemical potencies. Direct evidence estimates can be verified in the future, unlike predictive inference estimates which cannot be verified without additional information (i.e. indirect evidence and inference).

5.1.3 Indirect to Predictive

Some of the most interesting comparisons occur between indirect evidence and inference, and predictive inference. The overlap between these two sources of knowledge is small but important. Chemical risks, and specifically carcinogenic chemical risks, studied in predictive inference is only one small part of indirect evidence and inference. However, most of the chemicals studied to generate predictive inference have no equivalent or comparable human-based information. The overlap occurs where both epidemiology and toxicological risk assessment have been used to evaluate the risk posed by a chemical.

Nelson (1988) summarized some of the limitations and advantages of epidemiology and toxicological risk assessment (Table 5.1). The major advantage of epidemiology is its

relevance to humans, however there are many limitations in conducting epidemiological studies of environmental chemicals. The major disadvantage of toxicological risk assessment is its lack of relevance to humans, however there is very good control of many variables.

Table 5.1 Comparison of Epidemiology and Toxicological Risk Assessment

Most of the substances that have been identified as human carcinogens, based on epidemiological evidence, have also been shown to be experimental animal carcinogens. Of the 57 chemicals listed by the IARC as being associated with human cancer (Table 3.12) only five have not been shown to be carcinogenic in animal studies. They are alcoholic beverages (ethanol), oral contraceptives (sequential), smokeless tobacco products, talc containing asbestiform fibres and treosulfan (Vainio et al., 1993). These findings support the use of animals studies to predict human cancer even though it is unjustified to conclude that most laboratory animal carcinogens are also human carcinogens.

Higginson points out the difficulty of using epidemiology to detect the relatively low risks of most chemical health risks as well as the difficulty of 'negative' studies to refute chemical risks:

> "Even under favorable conditions, analytical epidemiological studies usually are insufficiently sensitive to detect cancer increases or decreases below 1 in 1000, except for certain rare tumors. A 'negative study', even with large numbers, will usually be compatible with a 20% increase in risk. The interpretation of 'negative' or weak associations in epidemiological investigations requires considerable scientific judgment and expertise ..." (Higginson, 1992, pg. 150)

For the 10 chemicals used in the predictive section (Section 4) to generate risk estimates in humans, four were based on potency factors that used human data (based on epidemiological studies) rather than laboratory animal carcinogens. This relatively high number of human based potency factors is due to the chemicals selected for the first priority substances list which sensibly focused on chemicals of most concern (and this concern was based on human effects). Only a handful of the hundreds of chemicals that have been tested for carcinogenicity have any supporting epidemiological information.

One of the most relevant analogies comparing indirect and predictive information was provided by Gough (1989). He used the Doll and Peto (1981) estimates of cancer deaths relating to environmental factors based on epidemiological information and U.S. EPA

Table 5.1 Comparison of Epidemiology and Toxicological Risk Assessment

Factor	Epidemiology	Toxicological Risk Assessment
Relevancy	Excellent	Uncertain
Control of Variables (exposure, environment and confounding factors)	Poor	Excellent
Identifying Causal Factors	Poor	Excellent
Size of Population	Can be large	Limited
Sensitivity	Poor	Poor
Genetic Diversity	Broad	Normally deliberately narrow
Intercurrent Disease	Not controllable	Controllable
Study of Mechanisms	Ethical hindrances, but directly relevant	Easily accessible, but uncertain relevancy
Diagnostic Tests	Severely restricted	Unrestricted

Nelson, 1988, Table 4-1

estimates of cancer incidence relating to environmental factors based (mostly) on toxicological risk assessment. Table 5.2 summarizes the comparisons. A conversion is needed because the U.S. EPA estimates were for developing cancer while the Doll and Peto estimates were for cancer mortality. Gough converted the cancer incidence to mortality by dividing the incidence by two. This conversion is based on the knowledge that approximately 50% of people die within 5 years of cancer diagnosis.

Table 5.2 Annual Cancer Mortality Associated with Environmental Exposures

The conclusion from Gough's analysis is that both epidemiological and toxicological risk assessment methods generate similar estimates for the major sources of cancer risk. It is reassuring that at a broad comparison of estimates from these two different sources of information could be reconciled.

Table 5.2 Annual Cancer Mortality Associated with Environmental Exposures

Study	Pollution*	Geophysical Factors*	Occupation*	Consumer Products*
Doll and Peto (range)	2% (<1-5%)	3% (2-4%)	4% (2-8%)	<1% (<1-2%)
U.S. EPA	1-3%	3-6%	<1-4%	<1%

Gough, 1989, Table 4

*Doll and Peto (1981) definitions:
Pollution - cancer from air pollution, water pollution and pesticide residues on food
Geophysical factors - cancer from UV radiation and ionizing radiation
Occupation - cancer from occupational exposures
Consumer Products - cancer from industrial products (e.g. detergents, paints, dyes)

5.2 Summary of Health Risk Evidence and Inference

This subsection will highlight some of the health risks based on direct evidence, indirect evidence and inference, and predictive inference.

Table 5.3 is a summary of mortality related parameters in Canada for 1993. Deaths, mortality rate, infant mortality and life expectancy are included. There were approximately 205,000 deaths in Canada in 1993 which averages out to approximately 560 deaths per day. Males continue to have greater number of deaths and mortality and subsequently a lower life expectancy by approximately 6 years compared to females.

Table 5.3 Summary of Parameters Related to Mortality, 1993

Table 5.4 is a summary of the major causes of death in Canada using 1993 information. Cardiovascular disease, cancer, respiratory disease and external causes (fatal injuries resulting from accidents, suicides and homicides) are the four leading causes of death, in the order listed, for both sexes. Infectious disease is no longer a leading cause of death in Canada but it was a major factor until earlier this century. Figure 2.26 and 2.27, shows the age-standardized death rates for the five major causes of death from 1930-1990. These figures, are based on thousands of pieces of information and summarize trends in mortality and health in recent Canadian history. Cardiovascular disease has remained the leading cause of death but has experienced two dramatic changes. Mortality increased for cardiovascular disease until approximately 1950 and then, gradually for males and immediately for females, they began to decrease significantly by approximately two fold. Cancer mortality rates have been increasing slightly for males while staying constant for females. Infectious diseases which had already declined significantly before 1930 continued to decline to low levels. The impact of HIV infection has begun to increase mortality levels, mostly in males to date. External causes have remained relatively stable over time with a small decrease starting around 1975.

Table 5.4 Summary of Major Causes of Death, 1993

Table 5.5 is a summary of the causes of death for the 17 categories from the ICD-9 code in Canada for 1993. Three methods are used to rank and compare the magnitude of the various causes of death: percent of total deaths, percent of potential years of life lost (PYLL @75) and loss of life expectancy (LLE). PYLL and LLE incorporate the age at death into

Table 5.3 Summary of Parameters Related to Mortality, 1993

Parameter	Males	Females
Deaths	109,407	95,505
Mortality Rate	7.63 deaths per 1,000	6.54 deaths per 1,000
Infant Mortality	6.3 per 1,000 live births	
Life Expectancy at Birth	74.9 years	81.0 years

Data Source: Statistics Canada, 1995a and 1996

Table 5.4 Summary of Major Causes of Death, 1993

Age Categories	Total Annual Deaths		% of Total Annual Deaths	
	Males	Females	Males	Females
Infectious Diseases	2,266	858	2.1	0.9
Cancer	30,970	26,211	28.3	27.4
Cardiovascular Diseases	40,513	38,381	37.0	40.2
Respiratory Diseases	9,971	8,082	9.1	8.5
External Causes	9,293	4,277	8.5	4.5
Other	16,394	17,696	15.0	18.5
All Causes	109,407	95,505	100	100

Data Source: Statistics Canada, 1995a

the calculations. PYLL places much greater weight on early deaths than LLE. The leading causes of deaths ranked using PYLL for males were external causes, cancer and cardiovascular diseases. For females they were cancer, external causes and cardiovascular disease. LLE shifted the various percentage but the cardiovascular disease and cancer remained the most significant for both sexes. The advantage of LLE however is that its numerical estimates are more useful for the individual than PYLL, in that LLE predicts the increase in life expectancy if the cause of death were eliminated.

Table 5.5 Causes of Death, 1993

Table 5.6 is a summary of the annual risk of dying by age and sex in Canada based on 1993 information. To aid in interpretation, the mortality rate values (deaths per 100,000) have been converted to chance and included in adjacent columns. For example, an annual mortality rate of 690 deaths per 100,000 in a year is equivalent to a 1 in 145 chance of dying in that year. Age is strongly and consistently associated with the risk of dying. In the early years of life (ages 5-9) the annual chance of dying is less than 1 in 5,000 while for later years (85+) the chance becomes greater than 1 in 10.

Table 5.6 Annual Risk of Dying by Age and Sex

Table 5.7 combines Tables 5.4 and 5.6. It shows the annual risk of dying by selected age, sex and major causes of death in Canada for 1993. Six age categories are used to present the range in mortality with age. Both death per 100,000 and chance of dying have been presented. This table highlights the substantially greater mortality risk for males for some causes of death (i.e. infectious because of AIDS, and external causes because of accidents and suicides).

Table 5.7 1993 Annual Risk of Dying by Selected Age, Sex and Major Cause of Death

So far only direct information has been presented. As shown by the large number of tables and figures in the direct section there is a substantial body of information available. Unfortunately similar summaries are not readily available for indirect evidence and inference. The following list highlights some available indirect health risk information, which is judged to be reliable:

- age is the overriding risk factor for most diseases. For example, assume that any hypothetical risk factor doubles your chances of dying from cardiovascular disease at

Table 5.5 Causes of Death, 1993

Cause of Death	Total		PYLL (@75 yrs)		LLE	
	Males	Females	Males	Females	Males	Females
Infectious Diseases	2.1 %	0.9 %	5.5 %	1 8 %	2.4 %	1.1 %
Cancer	28.3 %	27.4 %	22.5 %	36.8 %	28.2 %	33.2 %
Endocrine and Others	2.7 %	3.6 %	2.1 %	2.8 %	2.3 %	3.3 %
Blood Diseases	0.3 %	0.5 %	0.2 %	0.4 %	0.3 %	0.4 %
Mental Disorders	1.6 %	2.3 %	1.1 %	0.8 %	1.2 %	1.4 %
Nervous System Diseases	2.4 %	3.3 %	2.2 %	3.0 %	2.1 %	3.0 %
Cardiovascular Diseases	37.0 %	40.2 %	20.5 %	15.2 %	35.4 %	33.9 %
Respiratory Diseases	9.1 %	8.5 %	3.2 %	4.1 %	6.8 %	6.5 %
Digestive Diseases	3.6 %	3.8 %	3.4 %	3.1 %	3.2 %	3.4 %
Genito-Urinary Diseases	1.5 %	1.7 %	0.6 %	0.8 %	1.0 %	1.3 %
Pregnancy Related	- %	<0.1 %	- %	0.1 %	- %	<0.1 %
Skin Diseases	0.1 %	0.1 %	<0.1 %	0.1 %	<0.1 %	0.1 %
Musculo-Skeletal Diseases	0.2 %	0.6 %	0.1 %	0.6 %	0.2 %	0.6 %
Congenital Anomalies	0.6 %	0.5 %	3.4 %	5.1 %	1.4 %	1.8 %
Perinatal Conditions	0.6 %	0.5 %	4.1 %	5.4 %	1.7 %	1.8 %
Ill-Defined	1.5 %	1.6 %	3.6 %	3.8 %	1.9 %	1.8 %
External Causes	8.5 %	4.5 %	27.3 %	16.3 %	11.9 %	6.6 %

Data Source: Statistics Canada, 1995a

Table 5.6 Annual Risk of Dying by Age and Sex

Age Categories	Deaths per 100,000		Chance	
	Males	Females	Males	Females
<1	690	567	1 in 145	1 in 176
1-4	37	26	1 in 2,701	1 in 3,921
5-9	17	15	1 in 5,867	1 in 6,594
10-14	22	15	1 in 4,590	1 in 6,515
15-19	84	36	1 in 1,183	1 in 2,745
20-24	102	37	1 in 978	1 in 2,688
25-29	113	39	1 in 882	1 in 2,535
30-34	137	55	1 in 728	1 in 1,821
35-39	178	83	1 in 562	1 in 1,210
40-44	226	123	1 in 442	1 in 816
45-49	331	192	1 in 302	1 in 520
50-54	529	313	1 in 189	1 in 319
55-59	902	505	1 in 111	1 in 198
60-64	1,469	829	1 in 68	1 in 121
65-69	2,431	1,291	1 in 41	1 in 77
70-74	3,847	2,065	1 in 26	1 in 48
75-79	6,171	3,525	1 in 16	1 in 28
80-84	9,770	6,001	1 in 10	1 in 17
85-89	15,485	10,377	1 in 6	1 in 10
90+	22,773	19,777	1 in 4	1 in 5
All Ages	763	654	1 in 131	1 in 153

Data Source: Statistics Canada, 1995a

Table 5.7 1993 Annual Risk of Dying by Selected Age, Sex and Major Cause of Death

Infectious Diseases (Annual Risk)				
Age	Deaths per 100,000		Chance	
Categories	Males	Females	Males	Females
<1	7.0	10.1	1 in 14,267	1 in 9,929
5-9	0.2	0.7	1 in 501,643	1 in 137,533
25-29	11.8	1.8	1 in 8,470	1 in 56,242
45-49	22.5	2.7	1 in 4,451	1 in 37,700
65-69	23.2	12.6	1 in 4,308	1 in 7,966
85-89	125.1	66.7	1 in 800	1 in 1,499
All Ages	15.8	5.9	1 in 6,330	1 in 17,013
Cancer (Annual Risk)				
Age	Deaths per 100,000		Chance	
Categories	Males	Females	Males	Females
<1	7.5	5.3	1 in 13,316	1 in 18,865
5-9	3.4	3.3	1 in 29,508	1 in 30,085
25-29	8.1	8.0	1 in 12,359	1 in 12,565
45-49	89.3	107.1	1 in 1,119	1 in 934
65-69	938.5	581.2	1 in 107	1 in 172
85-89	3010.3	1515.2	1 in 33	1 in 66
All Ages	215.9	179.6	1 in 463	1 in 557
Cardiovascular Disease (Annual Risk)				
Age	Deaths per 100,000		Chance	
Categories	Males	Females	Males	Females
<1	10.0	5.3	1 in 9,987	1 in 18,865
5-9	0.8	0.7	1 in 125,411	1 in 137,533
25-29	4.0	2.6	1 in 24,718	1 in 38,099
45-49	91.6	27.1	1 in 1,091	1 in 3,696
65-69	928.7	388.8	1 in 108	1 in 257
85-89	7061.2	5412.2	1 in 14	1 in 18
All Ages	282.5	262.9	1 in 354	1 in 380
Respiratory Disease (Annual Risk)				
Age	Deaths per 100,000		Chance	
Categories	Males	Females	Males	Females
<1	10.5	13.3	1 in 9,512	1 in 7,546
5-9	0.2	0.5	1 in 501,643	1 in 192,546
25-29	1.2	1.4	1 in 86,514	1 in 73,817
45-49	7.2	5.4	1 in 13,869	1 in 18,480
65-69	171.1	83.1	1 in 585	1 in 1,203
85-89	2,349.3	1,073.6	1 in 43	1 in 93
All Ages	69.5	55.4	1 in 1,438	1 in 1,806

Table 5.7 1993 Annual Risk of Dying by Selected Age, Sex and Major Cause of Death (Continued)

External Causes (Annual Risk)				
Age Categories	Deaths per 100,000		Chance	
	Males	Females	Males	Females
<1	27.0	15.9	1 in 3,699	1 in 6,288
5-9	9.0	6.8	1 in 11,148	1 in 14,811
25-29	75.7	18.6	1 in 1,321	1 in 5,369
45-49	69.3	22.3	1 in 1,443	1 in 4,488
65-69	75.9	32.6	1 in 1,318	1 in 3,070
85-89	373.7	249.3	1 in 268	1 in 401
All Ages	64.8	29.3	1 in 1,543	1 in 3,413

Data Source: Statistics Canada, 1995a

all ages. For a male 25-29 the annual risk of dying from cardiovascular diseases is approximately 1 in 25,000 (Table 5.6) so doubling the risk yields approximately 1 chance in 12,500. For a male 65-69 the annual risk of dying from cardiovascular disease is approximately 1 in 110 so doubling that risk is approximately 1 in 55. The increased risk between the two age categories varies by a factor of 20 versus an increase of two for the hypothetical risk factor. So while this hypothetical risk factor is significant compared to many genuine risk factors, the age of the person is a more substantial factor with much greater certainty of effect.

- approximately 26% of male and 15% of female mortality has been attributed to smoking. Cancer and cardiovascular disease account for roughly equal proportions of smoking attributable mortality (approximately 40% each) while non-cancer respiratory diseases account for approximately 20% (Illing et al., 1995)
- diet has been shown to be an important determinant of health risk but few if any reliable quantitative estimates are available
- cancer - Doll and Peto (1981) provide a quantitative summary of risk factors which is still in line with more recent estimates (Table 3.15). Miller (1992) identifies some of principal factors associated with several types of cancer (Table 3.16).
- cardiovascular disease - estimated that as much as 30% of mortality is attributable to high blood pressure, 19% to diabetes, 17% to smoking and 15% to elevated serum cholesterol (Heart and Stroke Foundation of Canada, 1995)
- external causes - a significant fraction of all accidental deaths involved alcohol use. Approximately 40% of all motor vehicle fatalities were associated with blood alcohol levels over the legal limit and reasonable inferences would suggest that alcohol impairment plays a contributory role in many other types of fatal injuries

For predictive inference, there is very little information relating to human health risks . Table 4.8 summarizes the health risk estimates (intentionally cautious or over-estimates) for 10 chemicals at estimated average health levels of exposure to the specified chemicals for Canadians. At these average chemical exposure levels, the overall impacts on Canadians' health are predicted to be very low despite the intent to provide cautious estimates. Specific individual exposure situations however may have significantly higher exposures which would involve increased levels of risk to a small segment of the population.

Table 5.8 is a summary of annual mortality risks from the three different categories. Ideally, this table should have a big red CAUTION stamped on it because of all the

qualifications that are needed. The differences in evidentiary basis for the different estimates is very large as are the differences in uncertainty. The sections of the table were constructed as follows:

- direct evidence - the first four entries were taken from Tables 5.5 and 5.6, motor vehicle fatalities was based on approx. 3,500 deaths in 1993, lightning was based on an average of approx. 5 deaths/year for 1991-1994
- occupation - indirect evidence - based on values from Table 3.9, using the total occupation and the occupations with highest and lowest mortality rates
- recreation - indirect evidence - based on values from Table 3.11, selecting recreations that cover the range of mortality rates
- smoking - indirect evidence and inference - based on mortality rate (already expressed as deaths per 100,000) from Illing and Kaiserman (1995)
- predictive - based on values from Table 4.7. Because the values were for cancer incidence they were divided by two to get an estimate of the mortality as discussed earlier in the discussion. The highest and lowest of the ten chemicals in the table were selected in addition to benzene, between the extremes

Table 5.8 Annual Mortality Risks From Several Sources

All values were rounded to two significant figures for consistency despite the recognition that predictive risk estimates and those related to smoking are not reliable to more than one significant figure. Apart from the significant differences in uncertainty between the estimates, the other caution is that many of the estimates should logically not be expressed in terms of annual risks. Ideally all the estimates should also include age categories. Occupational, recreational and possibly lightning may be the most insensitive to the effects of age. Others like cancer, smoking and predictive inference (which are based on a risk estimated over a 70 year lifetime) must be interpreted with caution.

Table 5.8 Annual Mortality Risks From Several Sources

Source		Deaths per 100,000	Chance
Direct Evidence			
All Ages, All Causes of Death	Males	760	1 in 130
	Females	650	1 in 150
Ages 5-9, All Causes of Death	Males	17	1 in 5,900
	Females	15	1 in 6,600
Ages 85-89, All Causes of Death	Males	15,000	1 in 6
	Females	10,000	1 in 10
All Ages, All Cancer Deaths	Males	220	1 in 460
	Females	180	1 in 560
Motor Vehicle (All)		12.5	1 in 8,000
Lightning		0.017	1 in 5,900,000
Occupation (Indirect Evidence)			
Total Occupation		7.3	1 in 13,700
Mining, quarrying and oil wells		90	1 in 1,100
Health and social services		0.5	1 in 200,000
Recreation (Indirect Evidence)			
Mountain Climbing - dedicated		600	1 in 170
Parachuting		180	1 in 570
Scuba Diving - amateur		42	1 in 2,400
Snowmobiling		13	1 in 7,600
Mountain Hiking		6.4	1 in 15,700
Skiing - racing		2.5	1 in 40,000
Smoking (Indirect Evidence and Inference)			
	Males	210	1 in 480
	Females	100	1 in 1,000
Predictive Inference			
Arsenic (inorganic)		0.35	1 in 290,000
Benzene		0.045	1 in 2,200,000
Dichloroethane		0.0017	1 in 59,000,000

Data Source: Statistics Canada, 1995; Halperin, 1993; Cohen, 1991; Illing et al. 1995; Table 4.7

CAUTION: these values should normally NOT be compared unless a complete explanation is included of how the estimates were generated and the relative uncertainty in different estimates. All of these annual risks are highly age dependent and when no age category is included in the estimate, variations of several orders of magnitude can be hidden.

5.3 Summary of Uncertainty

Table 5.9 summarizes the uncertainty estimates for the three categories of health risks. Care should be taken in interpreting the uncertainty estimates since they may not accurately portray the uncertainty for some health risks, especially for more specific parameters.

Table 5.9 Summary of Uncertainty

For indirect evidence and inference, the statistical confidence limits do not account for bias and confounding. It has been estimated that the actual range of the confidence limits should be at least twice as large as reported in the studies to account for bias and confounding (Shlyakhter et al., 1993). Estimates motor vehicle, recreational, occupational (acute) are more certain because they are based on indirect evidence unlike most other risk factors which must use inferential information as well.

Overall, uncertainty is related to how well and consistently an outcome can be measured. If everyone is included (direct evidence) then estimates with low uncertainty are possible. When only a subset of the population is measured (indirect evidence and inference) the uncertainty increases when the results are used to estimate risk in others. This is especially true when exposure situations are different. An extreme example is using laboratory animals to predict human health risks (predictive inference). Even though these estimates are highly uncertain, they do provide a method for evaluating health risks, which is superior to having no information at all.

Table 5.9 Summary of Uncertainty

Category	Parameter	Appraisal of Uncertainty in Estimates
Direct	total number of deaths (including separation by sex and age)	less than 0.1%
	population-based rates (not by cause of death)	less than 5% (overall population) less than 10% (age-specific)
	cause of death	less than 5% (major category level) less than 10% to greater than 50% (three digit ICD codes)
Indirect	motor vehicle, recreational, occupational (acute)	less than 10%
	smoking	plus or minus 15% for estimating total annual mortality greater than 15% for specific causes of death (for disease - lung cancer most certain)
	smoking - second hand smoke	greater than 10 times (i.e. 1000%) for lung cancer and significantly larger for other cancers
	diet	plus or minus 100% for estimating contribution to total cancer mortality (less for some specific cancers) significantly larger for non-cancer mortality
	societal	less than 25% (quantitative estimates of education, level of income) greater than 100% (occupation) stress - currently unknown
	environmental	less than 25% to several factors of 10
Predictive	selection of model	from two orders of magnitude (10^2) to over eight orders of magnitude (10^8)
	overall toxicological risk assessment	larger than uncertainty in selection of model

Based on Sections 2, 3 and 4 of this thesis

CAUTION: care should be taken in interpreting the uncertainty estimates since they may not accurately portray the uncertainty for some health risks, especially for more specific parameters.

6. CONCLUSIONS AND RECOMMENDATIONS

6.1 Conclusions

6.1.1 Direct Evidence

- a large and reliable source of health risk information is available from death certificates. Detailed knowledge of recent health outcomes as well as reliable evidence on historical trends is available
- life expectancy has experienced a significant increase in the last 65 years. A large part of this increase can be attributed to decreases in infant mortality
- a dramatic decline in infectious disease mortality has occurred this century
- an exponential increase in mortality with age starts following the first few years of life. Infant mortality (under the age of 1), though significantly lower than in the past, has a mortality rate comparable to adults in their fifties
- there are consistent and often large differences in mortality rates between sexes, with males having a higher mortality rate for most causes of death compared with females
- the percentage of total deaths is commonly used to summarize the causes of death. Two additional measures, called potential years of life lost (PYLL) and loss of life expectancy (LLE) incorporate the relative age at death, thereby placing greater impact on premature deaths
- Statistics Canada should continue to include marital status evidence in its publications
- very low uncertainty is associated with direct information. Identifying the cause of death is the most uncertain piece of evidence

6.1.2 Indirect Evidence and Inference

- there are few quantitative summaries of the health risks associated with major risk factors. Interactions between major risk factors makes estimating risk for individual risk factors more difficult
- age is the most significant risk factor relating to mortality. Annual mortality rates vary over three orders of magnitude with age

- smoking is the most significant modifiable risk factor for smokers. A large fraction of all cancer, cardiovascular disease and respiratory disease mortality is associated with smoking
- a diet high in fruits and especially vegetables has consistently been linked with lower mortality for several causes of death. Lowered fat intake, especially saturated fat, is associated with a lower mortality risk
- alcohol is associated with many types of accidents including almost half of motor vehicle fatalities
- many effects associated with societal risk factors (such as level of income and education) are related to lifestyle/behavioural risk factors
- specific environmental risk factors (e.g. chemical contamination in air, water or food) have small and weak associations with human mortality compared with the major identified risk factors in Canada
- multiple risk factors can significantly increase the relative risk of mortality. Conversely, many people die from causes without any of the measurable risk factors.
- uncertainty varies tremendously among different risk factors because of the differing quality of evidence and strength of association

6.1.3 Predictive Inference

- of the 10 chemicals that were analyzed based on the priority substances list, the overall estimates of lifetime cancer risks at current background levels are very low. This occurred even though the estimates are conservative
- other exposure situations (e.g. certain occupations) can have substantially higher risk estimates
- the uncertainties are so large that methods which only rank the relative risk of chemicals may be more appropriate than making quantitative estimates of risks in humans

6.1.4 General

- misuse of numerical risk estimates is common
- risk perception studies have consistently shown that probability estimates (chances of death) are often only one component involved in making personal decisions about risk

- competing health claims are often misleading and/or unjustified. While the need for continued research into health risks is vital, the current reporting of individual research studies through popular media can misinform because the public because the information is not placed in the proper context
- separating health risk information by the source of evidence and the resulting inferential process helps in characterizing and understanding the types and level of uncertainty

6.2 Recommendations

- the dominance of age as an independent risk factor and its association with other major risk factors needs to be more widely acknowledged
- more dissemination of and access to health risk information in understandable forms is required

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Appendix 1 Detailed Causes of Death, 1993

Appendix 1 Detailed Causes of Death, 1993

Class	ICD-9 #	Name	Male	Female	Total
I	**001-139**	**Infectious and Parasitic Diseases**	**2,266**	**858**	**3,124**
	001-009	Intestinal Infectious Diseases	28	22	50
	010-018	Tuberculosis	67	50	117
	020-027	Zoonotic Bacterial Diseases	3	0	3
	030-041	Other Bacterial Diseases	424	485	909
	036	- Meningococcal Infection	17	22	39
	038	- Septicaemia	385	453	838
	042-044	Human Immunodeficiency Virus (HIV) Infection	1,474	90	1,564
	045-049	Polio, Non-Arthropod-Borne Viral Diseases Central Nervous System	25	25	50
	050-057	Viral Accompanied by Exanthem	21	24	45
	060-066	Arthropod-Borne Diseases	0	0	0
	070-079	Other Diseases Due to Viruses and Chlamydiae	99	62	161
	080-088	Rickettsioses and Other Arthropod-Borne Diseases	0	0	0
	090-099	Syphilis and Other Venereal Diseases	4	4	8
	100-104	Other Spirochaetal Diseases	0	0	0
	110-118	Mycoses	28	20	48
	120-129	Helminthiases	1	1	2
	130-136	Other Infectious and Parasitic Diseases	48	36	84
	135	- Sarcoidosis	18	16	34
	137-139	Late Effects of Infectious and Parasitic Diseases	48	36	84
	137	- Late Effects of Tuberculosis	26	25	51

Appendix 1 Detailed Causes of Death, 1993 - Continued

Class	ICD-9 #	Name	Male	Female	Total
II	**140-239**	**Neoplasms**	**30,970**	**26,211**	**57,181**
	140-149	Malignant Neoplasms of Lip, Oral Cavity and Pharynx	722	272	994
	141	- Malignant Neoplasm of Tongue	176	68	244
	150-159	Malignant Neoplasm of Digestive Organs and Peritoneum	8,073	6,941	15,014
	150	- Malignant Neoplasm of Oesophagus	795	338	1,133
	151	- Malignant Neoplasm of Stomach	1,211	778	1,989
	153	- Malignant Neoplasm of Colon	2,271	2,262	4,533
	154	- Malignant Neoplasm of Rectum, Rectosigmoid Junction and Anus	815	591	1,406
	155	- Malignant Neoplasm of Liver and Intrahepatic Bile Ducts	626	387	1,013
	157	- Malignant Neoplasm of Pancreas	1,403	1,407	2,810
	160-165	Malignant Neoplasm of Respiratory System	10,515	5,281	15,796
	161	- Malignant Neoplasm of Larynx	411	86	497
	162	- Malignant Neoplasm of Trachea, Bronchus and Lung	9,983	5,130	15,113
	170-175	Malignant Neoplasm, Bone, Connective Tissue, Skin and Breast	704	5,299	6,003
	172	- Malignant Melanoma of Skin	323	239	562
	174	- Malignant Neoplasm of Female Breast	0	4,779	4,779
	175	- Malignant Neoplasm of Male Breast	42	0	42
	179-189	Malignant Neoplasm of Genitourinary Organs	5,270	3,243	8,513
	183	- Malignant Neoplasm of Ovary and Other Uterine Adnexa	0	1,304	1,304
	185	- Malignant Neoplasm of Prostate	3,582	0	3,582
	188	- Malignant Neoplasm of Bladder	872	388	1,260
	189	- Malignant Neoplasm of Kidney and Other and Unspecified Urinary Organs	758	455	1,213
	190-199	Malignant Neoplasm of Other and Unspecified Sites	2,523	2,337	4,860
	191	- Malignant Neoplasm of Brain	733	553	1,286
	199	- Malignant Neoplasm Without Specification of Site	1,594	1,490	3,084
	200-208	Neoplasms of Lymphatic and Haematopoietic Tissue	2,676	2,336	5,012
	201	- Hodgkin's Disease	91	72	163
	202	- Other Malignant Neoplasm of Lymphoid and Histiocytic Tissue	895	862	1,757
	203	- Multiple Myeloma and Immunoproliferative Neoplasms	870	837	1,707
	204	- Lymphoid Leukaemia	366	247	613
cont'd	205	- Myeloid Leukaemia	419	332	751

Appendix 1 Detailed Causes of Death, 1993 - Continued

II cont'd	208	- Leukaemia of Unspecified Cell Type	283	260	543
	210-229	Benign Neoplasms	45	95	140
	225	- Benign Neoplasm of Brain and Other Parts of Nervous System	34	64	98
	230-234	Carcinoma In Situ	0	0	0
	235-238	Neoplasm of Uncertain Behaviour	211	189	400
	239	Neoplasm of Unspecified Nature	231	217	448
	239.6	- Brain	156	136	292

Class	ICD-9 #	Name	Male	Female	Total
III	**240-279**	**Endocrine, Nutritional and Metabolic Diseases and Immunity Disorders**	**2,955**	**3,425**	**6,380**
	240-246	Diseases of Thyroid Gland	20	88	108
	250-259	Diseases of Other Endocrine Glands	2,366	2,726	5,092
	250	- Diabetes Mellitus	2,339	2,682	5,021
	260-269	Nutritional Deficiencies	72	102	174
	270-279	Other Metabolic Disorders and Immunity Disorders	497	509	1,006
	276	- Disorders of Fluid, Electrolyte and Acid-Base Balance	194	249	443

Class	ICD-9 #	Name	Male	Female	Total
IV	**280-289**	**Diseases of Blood and Blood-Forming Organs**	**373**	**448**	**821**
	280-285	Anaemias	213	318	531
	284	- Aplastic Anaemia	83	83	166
	286-289	Other	160	130	290

Class	ICD-9 #	Name	Male	Female	Total
V	**290-319**	**Mental Disorders**	**1,800**	**2,234**	**4,034**
	290-294	Organic Psychotic Conditions	663	1,045	1,708
	290	- Senile and Presenile Organic Psychotic Conditions	593	1,031	1,624
	295-299	Other Psychoses	375	662	1,037
	295	- Schizophrenic Psychoses	35	39	74
	300-316	Neurotic, Personality and Other Non Psychotic Mental Disorders	738	507	1,245
	303	- Alcohol Dependence Syndrome	443	131	574
	310	- Specific Nonpsychotic mental Disorders Following Organic Brain Damage	141	264	405
	317-319	Mental Retardation	24	20	44

Appendix 1 Detailed Causes of Death, 1993 - Continued

Class	ICD-9 #	Name	Male	Female	Total
VI	320-389	**Diseases of the Nervous System and Sense Organs**	**2,586**	**3,153**	**5,739**
	320-326	Inflammatory Diseases of the Central Nervous System	44	52	96
	330-337	Hereditary and Degenerative Diseases of Nervous System	1,842	2,487	4,329
	331.0	- Alzheimer's Disease	849	1,563	2,412
	332	- Parkinson's Disease	540	470	1,010
	335	- Anterior Horn Cell Disease	263	266	529
	340-349	Other Disorders of Central Nervous System	546	504	1,050
	340	- Multiple Sclerosis	115	175	290
	345	- Epilepsy	157	96	253
	350-359	Disorders of the Peripheral Nervous System	151	105	256
	359	- Muscular Dystrophies and Other Myophapthies	106	63	169
	360-379	Disorders of the Eye and Adnexa	1	3	4
	380-389	Diseases of the Ear and Mastoid Process	2	2	4

Class	ICD-9 #	Name	Male	Female	Total
VII	390-459	**Diseases of the Circulatory System**	**40,513**	**38,381**	**78,894**
	390-392	Acute Rheumatic Fever	5	4	9
	393-398	Chronic Rheumatic Heart Disease	142	367	509
	401-405	Hypertensive Disease	532	775	1,307
	410-414	Ischaemic Heart Disease	25,101	19,667	44,768
	410	- Acute Myocardial Infarction	13,641	9,568	23,209
	414.0	- Coronary Atherosclerosis	5,692	5,600	11,292
	415-417	Diseases of Pulmonary Circulation	413	467	880
	420-429	Other Forms of Heart Disease	4,896	5,403	10,299
	427	- Cardiac Dysrhythmias	1,383	1,518	2,901
	428	- Heart Failure	1,791	2,380	4,171
	430-438	Cerebrovascular Disease	6,478	8,951	15,429
	436	- Acute But Ill-Defined Cerebrovascular Disease	3,792	5,551	9,343
	440-448	Diseases of Arteries, Arterioles and Capillaries	2,727	2,492	5,219
	440	- Atherosclerosis	784	1,180	1,964
	441	- Aortic Aneurysm	1,367	765	2,132
	451-459	Diseases, Veins, Lymphatics, Other Diseases Circulatory System	219	253	472

Appendix 1 Detailed Causes of Death, 1993 - Continued

Class	ICD-9 #	Name	Male	Female	Total
VIII	**460-519**	**Diseases of the Respiratory System**	**9,971**	**8,082**	**18,053**
	460-466	Acute Respiratory Infections	42	43	85
	470-478	Other Diseases of Upper Respiratory Tract	13	14	27
	480-487	Pneumonia and Influenza	3,288	3,759	7,047
	485	- Bronchopneumonia, Organism Unspecified	665	883	1,548
	486	- Pneumonia, Organism Unspecified	2,401	2,639	5,040
	487	- Influenza	85	152	237
	490-496	Chronic Obstructive Pulmonary Disease and Allied Conditions	5,573	3,326	8,899
	492	- Emphysema	770	370	1,140
	493	- Asthma	189	280	469
	496	- Chronic Airways Obstruction, NEC	4,257	2,374	6,631
	500-508	Pneumoconiosis, Other Lung Diseases Due to External Agents	283	248	531
	*** 500	- Coalworkers' Pneumoconiosis	0	1	1
	*** 501	- Asbestosis	16	0	16
	*** 502	- Pneumoconiosis Due to Other Silica or Silicates	21	0	21
	510-519	Other Diseases of Respiratory System	772	692	1,464
	515	- Postinflammatory Pulmonary Fibrosis	314	253	567

*** - included for interest

Class	ICD-9 #	Name	Male	Female	Total
IX	**520-579**	**Diseases of the Digestive System**	**3,931**	**3,624**	**7,555**
	520-529	Diseases of Oral Cavity, Salivary Glands and Jaws	0	8	8
	530-537	Diseases of Oesophagus, Stomach and Duodenum	445	433	878
	540-543	Appendicitis	21	19	40
	550-553	Hernia of Abdominal Cavity	80	82	162
	555-558	Noninfective Enteritis and Colitis	360	565	925
	560-569	Other Diseases of Intestines and Peritoneum	532	859	1,391
	560	- Intestinal Obstruction Without Mention of Hernia	220	329	549
	570-579	Other Diseases of Digestive System	2,493	1,658	4,151
	571	- Chronic Liver Disease and Cirrhosis	1,469	768	2,237
	578	- GI Haemorrhage	388	364	752

Appendix 1 Detailed Causes of Death, 1993 - Continued

Class	ICD-9 #	Name	Male	Female	Total
X	**580-629**	**Diseases of the Genito-Urinary System**	**1,607**	**1,647**	**3,254**
	580-589	Nephritis, Nephrotic Syndrome and Nephrosis	1,237	1,174	2,411
	585	- Chronic Renal Failure	365	337	702
	586	- Renal Failure, Unspecified	677	681	1,358
	590-599	Other Diseases of Urinary System	301	449	750
	600-608	Diseases of Male Genital Organs	69	0	69
	600	- Hyperplasia of Prostate	49	0	49
	610-611	Disorders of Breast	0	0	0
	614-616	Inflammatory Diseases of Female Pelvic Organs	0	11	11
	617-629	Other Disorders of Female Genital Tract	0	13	13

Class	ICD-9 #	Name	Male	Female	Total
XI	**630-676**	**Complications of Pregnancy, Childbirth and the Puerperium**	**0**	**15**	**15**
	630-639	Pregnancy With Abortive Outcome	0	1	1
	640-648	Complications Mainly Related to Pregnancy	0	10	10
	642	- Hypertension Complicating Pregnancy, Childbirth and the Puerperium	0	5	5
	650-659	Normal Delivery, and Other Indications for Care in Pregnancy, Labour and Delivery	0	0	0
	660-669	Complications Occurring in Labour and Delivery	0	1	1
	670-676	Complications of the Puerperium	0	3	3

Class	ICD-9 #	Name	Male	Female	Total
XII	**680-709**	**Diseases of the Skin and Subcutaneous Tissue**	**67**	**104**	**171**
	680-686	Infections of Skin and Subcutaneous Tissue	27	33	60
	690-698	Other Inflammatory Conditions, Skin and Subcutaneous Tissue	12	15	27
	700-709	Other Diseases of Skin and Subcutaneous Tissue	28	56	84
	707	- Chronic Ulcer of Skin	27	55	82

Appendix 1 Detailed Causes of Death, 1993 - Continued

Class	ICD-9 #	Name	Male	Female	Total
XIII	**710-739**	**Diseases of the Musculo-Skeletal System and Connective Tissue**	**213**	**593**	**806**
	710-719	Arthropathies and Related Disorders	148	431	579
	710	- Diffuse Diseases of Connective Tissue	39	144	183
	714.0	- Rheumatoid Arthritis	47	181	228
	720-724	Dorsopathies	9	11	20
	725-729	Rheumatism, Excluding the Back	13	17	30
	730-739	Other Diseases of the Musculo-Skeletal System	43	134	177

Class	ICD-9 #	Name	Male	Female	Total
XIV	**740-759**	**Congenital Anomalies**	**603**	**525**	**1,128**
	740-742	Nervous System	68	84	152
	745-747	Circulatory System	263	216	479
	746	- Other Congenital Anomalies of Heart	136	104	240
	748-749	Respiratory System	62	44	106
	750-751	Digestive System	18	13	31
	752-753	Genitourinary System	37	34	71
	754-756	Limbs and Musculo-Skeletal System	42	30	72
	757-759	Other	112	104	216
	758	- Chromosomal Anomalies	67	71	138

Class	ICD-9 #	Name	Male	Female	Total
XV	**760-779**	**Certain Conditions Originating in the Perinatal Period (Excluding Stillbirths)**	**615**	**440**	**1,055**
	761	- Fetus or Newborn Affected by Maternal Complications of Pregnancy	64	52	116
	762	- Fetus or Newborn Affected by Complications of Placenta, Cord and Membranes	59	49	108
	765	- Disorders Relating to Short Gestation and Unspecified Low Birthweight	107	81	188
	770	- Other Respiratory Conditions of Fetus or Newborn	111	57	168

Appendix 1 Detailed Causes of Death, 1993 - Continued

Class	ICD-9 #	Name	Male	Female	Total
XVI	**780-799**	**Symptoms, Signs and Ill-Defined Conditions**	**1,644**	**1,488**	**3,132**
	780-789	Symptoms	65	70	135
	785.5	- Shock Without Mention of Trauma	20	32	52
	790-796	Nonspecific Abnormal Findings	2	2	4
	797-799	Ill-Defined and Unknown Causes of Morbidity and Mortality	1,577	1,416	2,993
	798.0	- Sudden Infant Death Syndrome	142	126	268
	799.9	- Other Unknown and Unspecified Cause	1,264	954	2,218

Class	ICD-9 #	Name	Male	Female	Total
E XVII	**E800-E999**	**External Causes, Injury and Poisoning**	**9,293**	**4,277**	**13,570**
	E800-E807	Railway Accidents	32	6	38
	E805	- Hit by Rolling Stock	29	6	35
	E810-E819	Motor Vehicle Traffic Accidents	2,311	1,108	3,419
	E810	- Motor Vehicle Traffic Accident Involving Collision With Train	36	8	44
	E812	- Other Motor Vehicle Traffic Accident Involving Collision With Another Vehicle	832	504	1,336
	E814	- Motor Vehicle Traffic Accident Involving Collision With Pedestrian	244	175	419
	E816	- Motor Vehicle Traffic Accident Due to Loss of Control, Without Collision on the Highway	418	118	536
	E819	- Motor Vehicle Traffic Accident of Unspecified Nature	403	197	600
	E820-E825	Motor Vehicle Nontraffic Accidents	112	12	124
	E820	- Nontraffic Accident Involving Motor-Driving Snow Vehicle	65	6	71
	E826-E829	Other Road Vehicle Accidents	19	7	26
	E826	- Pedal Cycle Accident	12	2	14
	E828	- Accident Involving Animal Being Ridden	4	5	9
	E830-E838	Water Transport Accidents	127	9	136
	E830	- Accident to Watercraft Causing Submersion	77	4	81
	E840-E845	Air and Space Transport Accidents	81	9	90
	E840	- Accident to Powered Aircraft at Takeoff or Landing	10	2	12
	E841	- Accident to Powered Aircraft, Other and Unspecified	65	6	71
	E846-E848	Vehicle Accidents Not Elsewhere Classifiable	4	0	4
	E850-E858	Accidental, Poisoning, Drugs, Medicaments, Biologicals	482	199	681
cont'd	E850.0	- Opiates and Related Narcotics	197	42	239

Appendix 1 Detailed Causes of Death, 1993 - Continued

E XVII cont'd	E860-E869	Accidental Poisoning by Other Substances	160	41	201
	E860	- Accidental Poisoning by Alcohol, NEC	79	26	105
	E868	- Accidental Poisoning by Other Utility Gas and Other Carbon Monoxide	59	5	64
	E870-E876	Misadventures to Patients During Surgical and Medical Care	11	17	28
	E870	- Accidental Cut, Puncture, Perforation or Haemorrhage During Medical Care	7	13	20
	E878-E879	Complication of Medical Procedures Without Mention of Misadventure	68	70	138
	E880-E888	Accidental Falls	1,023	1,215	2,238
	E887	- Fracture, Cause Unspecified	387	678	1,065
	E888	- Other and Unspecified Fall	280	343	623
	E890-E899	Accidents Caused by Fire and Flames	217	122	339
	E890	- Conflagration in Private Dwelling	182	105	287
	E900-E909	Accidents Due to Natural and Environmental Factors	88	39	127
	E901	- Excessive Cold	64	26	90
	*** E907	- Lightning	1	0	1
	E910-E915	Accidents, Submersion, Suffocation and Foreign Bodies	505	235	740
	E910	- Accidental Drowning and Submersion	287	65	352
	E916-E928	Other Accidents	440	93	533
	E916	- Struck Accidentally by Falling Object	83	6	89
	E919	- Accidents Caused by Machinery	132	9	141
	E922	- Accident Caused by Firearm Missile	42	2	44
	E925	- Accident Caused by Electric Current	29	2	31
	E929	Late Effects of Accidental Injury	49	32	81
	E930-E949	Substances Causing Adverse Effects in Therapeutic Use	7	18	25
	E950-E959	Suicide and Selfinflicted Injury	3,014	789	3,803
	E950	- ... poisoning by solid or liquid substances	279	290	569
	E952	- ... poisoning by other gases and vapours	382	79	461
	E953	- ... by hanging, strangulation and suffocation	1,011	223	1,234
	E954	- ... by submersion	97	42	139
	E955	- ... by firearms and explosives	993	61	1054
	E956	- ... by cutting and piercing instruments	66	14	80
	E957	- ... by jumping from high place	114	48	162
	E960-E969	Homicide and Injury Purposely Inflected by Other Persons	358	168	526
	E965	- Assault by Firearms and Explosives	131	44	175
	E966	- Assault by Cutting and Piercing Instrument	116	50	166
	E970-E978	Legal Intervention	5	0	5
	E980-E989	Injury Undetermined, Accidentally or Purposely Inflicted	180	88	268
	E990-E999	Injury Resulting from Operations of War	0	0	0

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*** - lighting include for interest

Appendix 2 Causes of Death by Age, 1993

Appendix 2 Causes of Death by Age, 1993

Deaths <1

	ICD-9	Shortened Cause Name	#	%	Rate[1]
Male	XV	Perinatal Conditions	609	44.2	304.9
	XIV	Congenital Anomalies	380	27.6	190.2
	XVI	Ill-Defined - Sudden Infant Death Syndrome	180	13.1	90.1
	E XVII	External Causes	54	3.9	27.0
	VI	Nervous System Diseases	34	2.8	19.5
		All Other	117	8.5	58.6
		Total	1,379	100.0	690.4
Female	XV	Perinatal Conditions	437	40.9	231.6
	XIV	Congenital Anomalies	330	30.9	174.9
	XVI	Ill-Defined - Sudden Infant Death Syndrome	155	14.5	82.2
	E XVII	External Causes	30	2.8	15.9
	VIII	Respiratory Diseases	25	2.3	13.3
		All Other	92	8.6	48.8
		Total	1,069	100.0	566.7

[1] Deaths per 100,000

Deaths 1-4

	ICD-9	Shortened Cause Name	#	%	Rate[1]
Male	E.XVII	External Causes	110	35.9	13.3
	XIV	Congenital Anomalies	53	17.3	6.4
	II	Cancer	34	11.1	4.1
	VIII	Respiratory Diseases	25	8.2	3.0
	VII	Cardiovascular Diseases	15	4.9	1.8
		All Other	69	22.5	8.3
		Total	306	100.0	37.0
Female	E XVII	External Causes	69	34.3	8.8
	XIV	Congenital Anomalies	29	14.4	3.7
	II	Cancer	21	10.4	2.7
	VIII	Respiratory Diseases	19	9.5	2.4
	VI	Nervous System Diseases	17	8.5	2.2
		All Other	46	22.9	5.8
		Total	201	100.0	25.5

[1] Deaths per 100,000

Appendix 2 Causes of Death by Age, 1993 - Continued

Deaths 5-14

	ICD-9	Shortened Cause Name	#	%	Rate[1]
Male	E XVII	External Causes	209	10.4	10.4
	II	Cancer	66	3.3	3.3
	VI	Nervous System Diseases	30	1.5	1.5
	VII	Cardiovascular Diseases	19	0.9	0.9
	XIV	Congenital Anomalies	15	0.7	0.7
		All Other	51	2.5	2.5
		Total	390	100.0	19.4
Female	E XVII	External Causes	131	44.7	6.8
	II	Cancer	61	20.8	3.2
	VI	Nervous System Diseases	20	6.8	1.0
	VII	Cardiovascular Diseases	16	5.5	0.8
	XIV	Congenital Anomalies	16	5.5	0.8
		All Other	49	16.7	2.6
		Total	293	100.0	15.3

[1] Deaths per 100,000

Deaths 15-24

	ICD-9	Shortened Cause Name	#	%	Rate[1]
Male	E XVII	External Causes	1,500	78.0	73.0
	II	Cancer	112	5.8	5.5
	XVI	Ill-Defined	60	3.1	2.9
	VI	Nervous System Diseases	58	3.0	2.8
	VII	Cardiovascular Diseases	49	2.5	2.4
		All Other	144	7.5	7.0
		Total	1,923	100.0	93.6
Female	E XVII	External Causes	457	62.7	23.1
	II	Cancer	86	11.8	4.3
	VI	Nervous System Diseases	30	4.1	1.5
	VII	Cardiovascular Diseases	28	3.8	1.4
	XVI	Ill-Defined	27	3.7	1.4
		All Other	101	13.9	5.1
		Total	729	100.0	36.8

[1] Deaths per 100,000

Appendix 2 Causes of Death by Age, 1993 - Continued

Deaths 25-34

	ICD-9	Shortened Cause Name	#	%	Rate[1]
Male	E XVII	External Causes	1,951	60.3	76.0
	I	Infectious Diseases	442	13.7	17.2
	II	Cancer	259	8.0	10.1
	VII	Cardiovascular Diseases	179	5.5	7.0
	XVI	Ill-Defined	137	4.2	5.3
		All Other	265	8.2	10.3
		Total	3,233	100.0	126.0
Female	E XVII	External Causes	487	40.9	19.5
	II	Cancer	301	25.3	12.0
	VII	Cardiovascular Diseases	95	8.0	3.8
	XVI	Ill-Defined	49	4.1	2.0
	I	Infectious Diseases	48	4.0	1.9
		All Other	211	17.7	8.4
		Total	1,191	100.0	47.6

[1] Deaths per 100,000

Deaths 35-44

	ICD-9	Shortened Cause Name	#	%	Rate[1]
Male	E XVII	External Causes	1,672	35.4	70.9
	VII	Cardiovascular Diseases	778	16.5	33.0
	II	Cancer	770	16.3	32.6
	I	Infectious Diseases	682	14.4	28.9
	IX	Digestive Diseases	201	4.3	8.5
		All Other	626	13.2	26.5
		Total	4,729	100.0	200.5
Female	II	Cancer	1,076	45.3	45.9
	E XVII	External Causes	534	22.5	22.8
	VII	Cardiovascular Diseases	279	11.7	11.9
	IX	Digestive Diseases	94	4.0	4.0
	VI	Nervous System Diseases	68	2.9	2.9
		All Other	324	13.6	13.8
		Total	2,375	100.0	101.4

[1] Deaths per 100,000

Appendix 2 Causes of Death by Age, 1993 - Continued

Deaths 45-54

	ICD-9	Shortened Cause Name	#	%	Rate[1]
Male	II	Cancer	2,243	31.8	132.7
	VII	Cardiovascular Diseases	2,138	30.3	126.5
	E XVII	External Causes	1,118	15.9	66.2
	IX	Digestive Diseases	366	5.2	21.7
	I	Infectious Diseases	343	4.9	20.3
		All Other	841	11.9	49.8
		Total	7,049	100.0	417.2
Female	II	Cancer	2,312	56.5	138.4
	VII	Cardiovascular Diseases	635	15.5	38.0
	E XVII	External Causes	387	9.5	23.2
	IX	Digestive Diseases	180	4.4	10.8
	VIII	Respiratory Diseases	132	3.2	7.9
		All Other	446	10.9	26.7
		Total	4,029	100.0	245.0

[1] Deaths per 100,000

Deaths 55-64

	ICD-9	Shortened Cause Name	#	%	Rate[1]
Male	II	Cancer	5,784	40.4	476.3
	VII	Cardiovascular Diseases	5,069	35.4	417.3
	E XVII	External Causes	764	5.3	62.9
	IX	Digestive Diseases	696	4.9	57.3
	VIII	Respiratory Diseases	684	4.8	56.3
		All Other	1,325	9.3	109.1
		Total	14,322	100.0	1,180.
Female	II	Cancer	4325	52.2	347.8
	VII	Cardiovascular Diseases	1964	23.7	157.9
	VIII	Respiratory Diseases	453	5.5	36.4
	IX	Digestive Diseases	317	3.8	25.5
	E XVII	External Causes	315	3.8	25.3
		All Other	908	11.0	73.0
		Total	8,282	100.0	666.0

[1] Deaths per 100,000

Appendix 2 Causes of Death by Age, 1993 - Continued

Deaths 65-74

	ICD-9	Shortened Cause Name	#	%	Rate[1]
Male	VII	Cardiovascular Diseases	10,899	39.1	1,194.
	II	Cancer	10,274	36.9	1,126.
	VIII	Respiratory Diseases	2,267	8.1	248.4
	IX	Digestive Diseases	1,032	3.7	113.1
	III	Endocrine and Others	824	3.0	90.3
		All Other	2,562	9.2	280.7
		Total	27,858	100.0	3,052.
Female	II	Cancer	7,489	41.0	678.0
	VII	Cardiovascular Diseases	6,182	33.9	559.6
	VIII	Respiratory Diseases	1,277	7.0	115.6
	III	Endocrine and Others	737	4.0	66.7
	IX	Digestive Diseases	712	3.9	64.5
		All Other	1,851	10.1	167.6
		Total	18,248	100.0	1,652.

[1] Deaths per 100,000

Deaths 75-84

	ICD-9	Shortened Cause Name	#	%	Rate[1]
Male	VII	Cardiovascular Diseases	13,602	43.3	3,252.
	II	Cancer	8,523	27.1	2,038.
	VIII	Respiratory Diseases	3,974	12.6	950.4
	IX	Digestive Diseases	980	3.1	234.4
	III	Endocrine and Others	927	3.0	221.7
		All Other	3,410	10.9	815.5
		Total	31,416	100.0	7,513.
Female	VII	Cardiovascular Diseases	13,285	45.7	2,075.
	II	Cancer	7,060	24.3	1,102.
	VIII	Respiratory Diseases	2,653	9.1	414.3
	III	Endocrine and Others	1,194	4.1	186.5
	IX	Digestive Diseases	1,102	3.8	172.1
		All Other	3,758	12.9	586.9
		Total	29,052	100.0	4,537.

[1] Deaths per 100,000

Appendix 2 Causes of Death by Age, 1993 - Continued

Deaths 85+

	ICD-9	Shortened Cause Name	#	%	Rate[1]
Male	VII	Cardiovascular Diseases	7,744	46.1	8,129.
	II	Cancer	2,890	17.2	3,034.
	VIII	Respiratory Diseases	2,671	15.9	2,804.
	IX	Digestive Diseases	568	3.4	596.2
	V	Mental Disorders	539	3.2	565.8
		All Other	2,387	14.2	2,506.
		Total	16,799	100.0	17,634.
Female	VII	Cardiovascular Diseases	15,880	53.0	7,243.
	II	Cancer	3,470	11.6	1,583.
	VIII	Respiratory Diseases	3,396	11.3	1,549.
	V	Mental Disorders	1,287	4.3	587.0
	IX	Digestive Diseases	1,172	3.9	534.6
		All Other	4,768	15.9	2175.
		Total	29,973	100.0	13,671.

[1] Deaths per 100,000

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Appendix 3 Factors Influencing Morbidity and Mortality

Appendix 3 Factors Influencing Morbidity and Mortality

Disease	HUMAN BIOLOGY				PRE-DISPOSING CONDITIONS							ENVIRONMENT			POLLUTION				LIFESTYLE						HEALTH CARE		
	Heredity/Family Hist.	Ethnic Group/Skin Color	Blood Group/HLA Type	Reproductive History	Blood Pressure	Cholesterol	Infection	Ulcer/Polyp	Trauma	Allergy	Socio Economic Status	Occupation	Housing	Air	Water	Food	Weather/UVR	Tobacco	Alcohol	Diet/Obesity	Physical Activity	Promiscuity	Car/Motorcycle	Stress	Early Detection	Drugs	x-Rays
A. Malignant Neoplasm																											
1. Buccal Cavity and Pharynx		+					?				+	+					+	+	+								
2. Esophagus												?						+	+	+							
3. Stomach		+	+					?			+				?	?	?	?	?	+							
4. Large intestine and rectum	+	+						+			+	?							?	+					+		
5. Pancreas																											
6. Trachea, bronchus and lung	?											+		+			+										
7. Melanoma of skin	+	+										?					-									?	
8. Other skin	+	+						+	?								-									+	-
9. Breast (female)	+							+			-									+					+	?	-
10. Cervix uteri		+		+			?				-											+			+		
11. Other uterus				+																+						+	
12. Ovary				+																							
13. Prostate		+		+			?					+								?		?					
14. Bladder							+	+				+						+		?							-
15. Other urinary organs	+						-		+			-		?				-									
16. Eye	+								?								?										
17. Brain and N.S.	?	?	+									?		?													-
18. Thyroid																				+							-
19. Non-Hodgkin's lymphoma	?	?					+					?														-	
20. Hodgkin's Disease	+						+					?															
21. Multiple myeloma												+															
22. Leukemia	+	?	?				?					+															
B. Other Diseases																											
23. Tuberculosis		+									+		+					?							+		
24. Polycythemia vera	?	?					?																				?
25. Uterine fibroma				?																							
26. Benign ovarian tumour				?																							
27. Thyrotoxicosis	+																							?		+	-
28. Myxecema	?																									+	-
29. Diabetes mellitus	+	+	+				?												+	+							
30. Gout	+																			+							
31. Hereditary neuromusc. dis.	+																										
32. Multiple sclerosis	+	+	+				?													?							
33. Paralysis agitans							+																			+	
34. Epilepsy	+						+		+																		
35. Motor neurone disease	?						?																				
36. Strabismus	?						?		?																		
37. Cataract	+						+		+																		

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Appendix 3 Factors Influencing Morbidity and Mortality (Continued)

	HUMAN BIOLOGY											ENVIRONMENT							LIFESTYLE								HEALTH CARE		
					PRE-DISPOSING CONDITIONS									POLLUTION																
	Heredity/Family Hist.	Ethnic Group/Skin Color	Blood Group/HLA Type	Reproductive History	Blood Pressure	Cholesterol	Infection	Ulcer/Polyp	Trauma	Allergy	Socio Economic Status	Occupation	Housing	Air	Water	Food	Weather/UVR	Tobacco	Alcohol	Diet/Obesity	Physical Activity	Promiscuity	Car/Motorcycle	Stress	Early Detection	Drugs	X-Rays
38. Glaucoma	?						?		?																				
39. Detachment of retina							?		+																				
40. Menière's disease							?		?																				
41. Otosclerosis	+																												
42. Chronic rehmuatic heart dis.							+				+																		
43. Hypertensive disease	+	+					+				+	+							+	+	+			+	+	+			
44. Ischemic heart disease	+	+			+	+									+		+	+	+	+	+			+					
45. Cerebro vascular disease	+				+	+														+					-				
46. Aortic aneurysm							+		+																				
47. Pulmonary embolism				+					+			+								+	+					+		
48. Brochitis, emphysema, asthma	+						+			+		+			+		+	+											
49. Deflected nasal sectum	+								+																				
50. Peptic ulcer											-	+						+						?					
51. Appednicitis							+													?									
52. Hernia	+								+			+																	
53. Intestinal obstruction w/o hernia	+						+																						
54. Ulcerative colitis	+						?																						
55. Cirrhosis of liver	+						+					+						+									+		
56. Gallbladder disease	+						+													+									
57. Pancreatic disease							+		+									+									+		
58. Nephritis and neophrosis	+						+					+															+		
59. Hydronephrosis							+		+																				
60. Renal calculus							+													+									
61. Prostatic hyperplasia				?																									
62. Ectopic pregnancy							+																						
63. Arthritis and rheumatism	+		+						+			+																	
64. Osteitis deformans	?																												
65. Osteochondrosis	+																			?									
66. Cong. Anomaly of Nerv. Syst.	+			+																?									
67. Cong. Anomaly of Circ. Syst.	+			+			+																						
68. Cleft palate, lip	+			+																									
69. Fracture of skull									+			+					+		+		+		+						
70. Fracture of spine									+			+					+		+		+		+						
71. Fracture of neck of femur									+				+				+			+	+						+		
72. Internal injury									+			+							+		+		+						
73. Burns												+	+				+		+										
74. Adverse effect of medical agents												+							+									+	
75. Toxic effect of non-medical subst.												+	+						+										

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